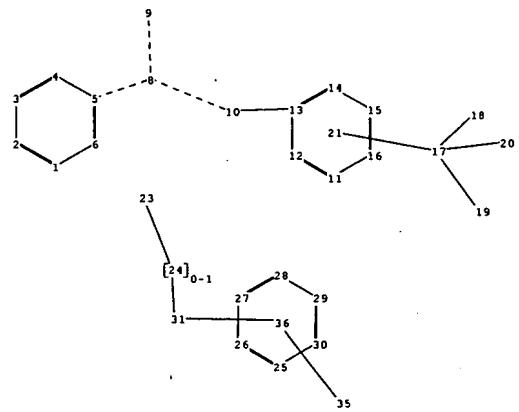
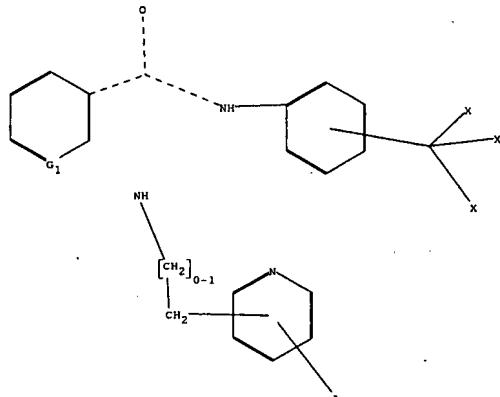


10 S38199



chain nodes :

8 9 10 17 18 19 20 23 24 31 35

ring nodes :

1 2 3 4 5 6 11 12 13 14 15 16 25 26 27 28 29 30

chain bonds :

5-8 8-9 8-10 10-13 17-18 17-19 17-20 23-24 24-31

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16 25-26 25-30
26-27 27-28 28-29 29-30

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-8 8-9 8-10 10-13 17-18 17-19 17-20 23-24 24-31

normalized bonds :

11-12 11-16 12-13 13-14 14-15 15-16 25-26 25-30 26-27 27-28 28-29 29-30

isolated ring systems :

containing 1 : 11 : 25 :

G1:N,CH

Match level :

 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 8:CLASS 9:CLASS 10:CLASS 11:Atom
 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS 20:CLASS
 21:Atom 23:CLASS 24:CLASS 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom
 31:CLASS 32:Atom 35:CLASS 36:Atom

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PASSWORD :

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NEWS 4 JUL 02 CHEMCATS accession numbers revised
NEWS 5 JUL 02 CA/CAplus enhanced with utility model patents from China
NEWS 6 JUL 16 CAplus enhanced with French and German abstracts
NEWS 7 JUL 18 CA/CAplus patent coverage enhanced
NEWS 8 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9 JUL 30 USGENE now available on STN
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NEWS 18 SEP 07 STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 19 SEP 13 FORIS renamed to SOFIS
NEWS 20 SEP 13 INPADOCDB enhanced with monthly SDI frequency
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NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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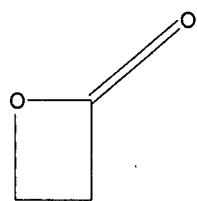
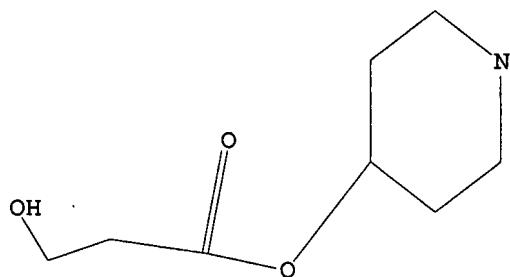
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L1 STRUCTURE UPLOADED

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L1 STR



Structure attributes must be viewed using STN Express query preparation.

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L2      STR
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *
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Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 16:53:53 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       660 TO ITERATE
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100.0% PROCESSED      660 ITERATIONS          8 ANSWERS
SEARCH TIME: 00.00.01
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FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:    11659 TO    14741
PROJECTED ANSWERS:        8 TO      329
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L3      8 SEA SSS SAM L2
```

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=> s 12 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 171.65 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
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Updated Search

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FULL SCREEN SEARCH COMPLETED - 13471 TO ITERATE

100.0% PROCESSED 13471 ITERATIONS
SEARCH TIME: 00.00.01

207 ANSWERS

L4 207 SEA SSS FUL L2

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COST IN U.S. DOLLARS		ENTRY	SESSION
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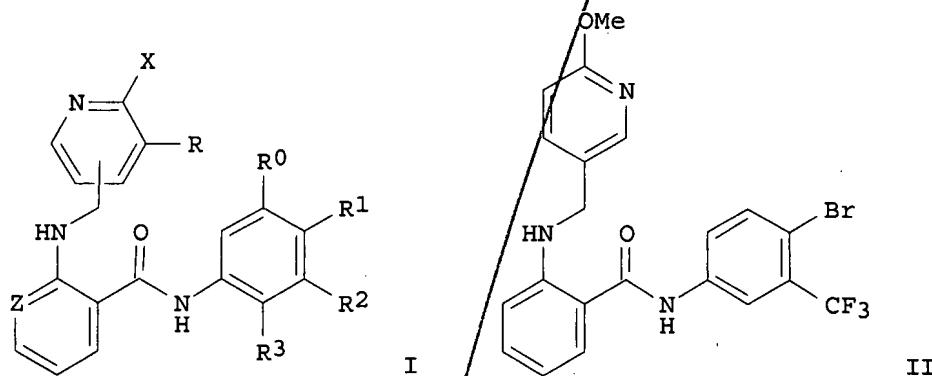
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100 BOLD, G?/AU
L6 5 L5 AND BOLD, G?/AU

=> d 16, ibib abs hitstr, 1-5

L6 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER.: 2004:515506 HCAPLUS
DOCUMENT NUMBER: 141:71453
TITLE: Preparation of anthranilic acid amide derivatives as neoplastic inhibitors
INVENTOR(S): Bold, Guido; Furet, Pascal; Manley, Paul William
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052884	A1	20040624	WO 2003-EP14086	20031211
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RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2506164	A1	20040624	CA 2003-2506164	20031211
AU 2003294834	A1	20040630	AU 2003-294834	20031211
EP 1572686	A1	20050914	EP 2003-785795	20031211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017292	A	20051108	BR 2003-17292	20031211
CN 1720244	A	20060111	CN 2003-80104845	20031211
JP 2006511518	T	20060406	JP 2004-558075	20031211
US 2006128684	A1	20060615	US 2005-538199	20050609
PRIORITY APPLN. INFO.:			GB 2002-29022	A 20021212
			WO 2003-EP14086	W 20031211

OTHER SOURCE(S) : MARPAT 141:71453
GI



AB The title compds. I [wherein R and R₀ = independently H, halo, (un)substituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, etc.; R₁ = H, halo, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, OCF₃, OCH₂CF₃, OCH₂CH₂CF₃, or OCH₂CH₂CH₂CF₃; R₂ = perfluoroalkyl; R₃ = H or halo; X = OH, alkoxy, alkylthio, imino, alkylimino, halo, etc.; Z = N or CH] or salts, N-oxides, or tautomers thereof are prepared as neoplastic inhibitors for the treatment of human or animal body. For example, the compound II was prepared in a multi-step synthesis. Formulations containing I as an active ingredient were also described.

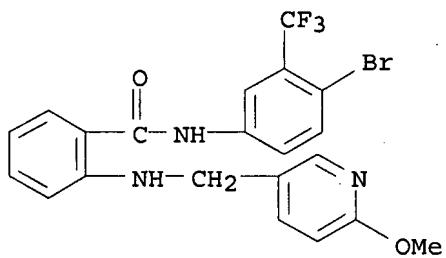
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	709045-04-5P	709045-05-6P	709045-08-9P
	709045-10-3P	709045-11-4P	709045-28-3P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate, reactant; preparation of anthranilic acid amide derivs. as

neoplastic inhibitors)

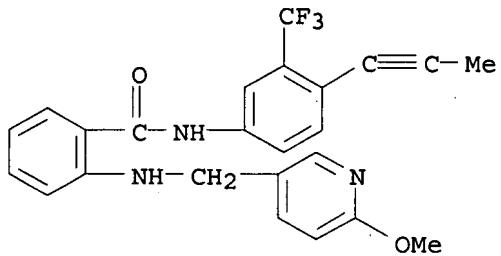
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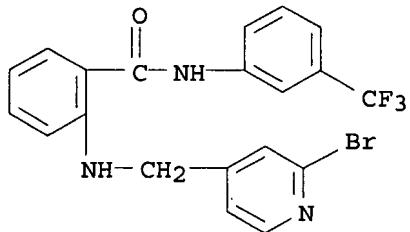
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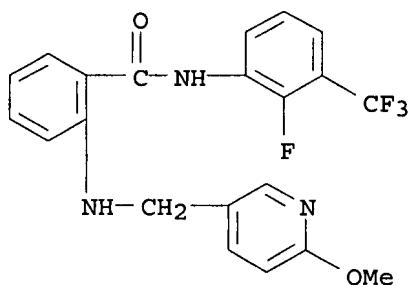
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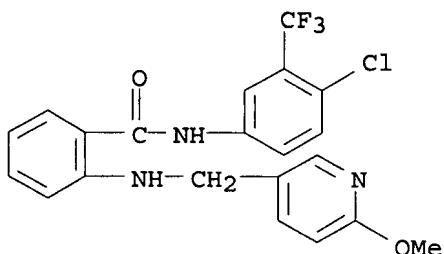
RN 709044-84-8 HCAPLUS

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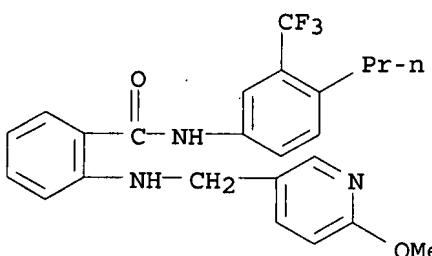
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RN 709044-88-2 HCPLUS

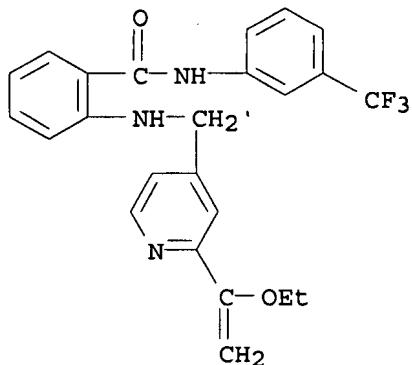
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●x HCl

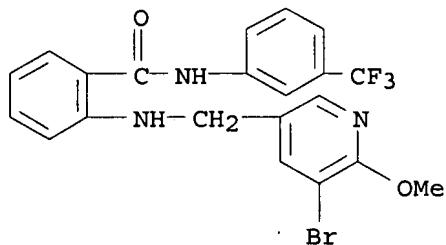
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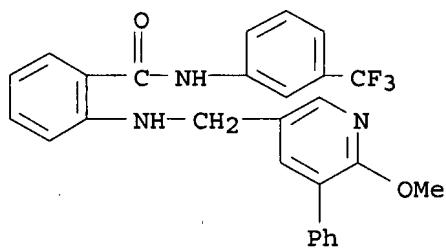
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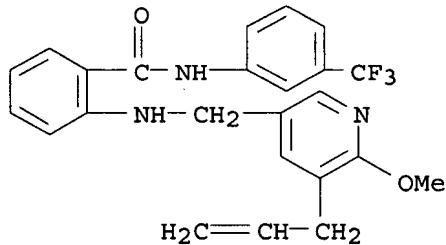
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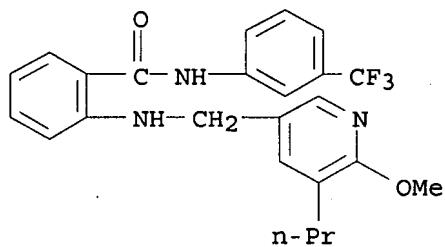
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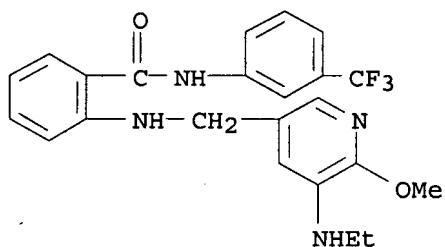


Updated Search

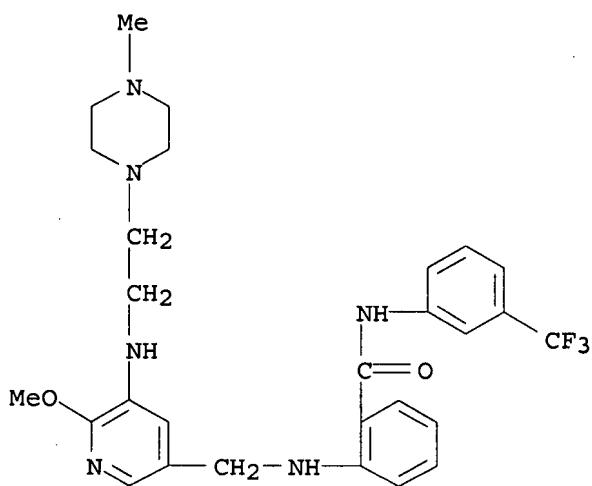
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RN 709045-08-9 HCAPLUS
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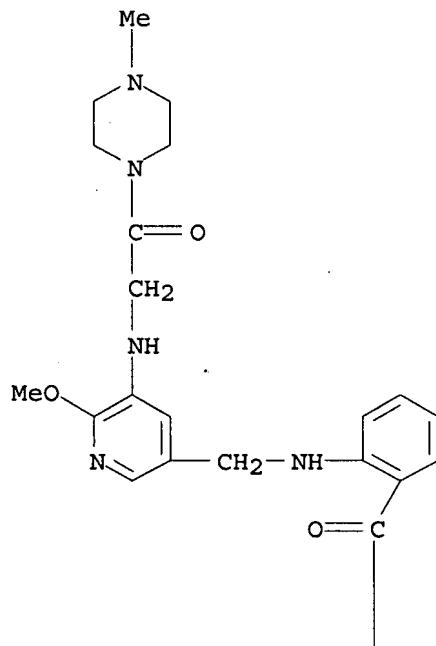


RN 709045-10-3 HCAPLUS
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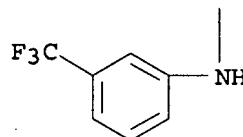


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CN Benzamide, 2-[[[6-methoxy-5-[[2-(4-methyl-1-piperazinyl)-2-oxoethyl]amino]-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

PAGE 1-A

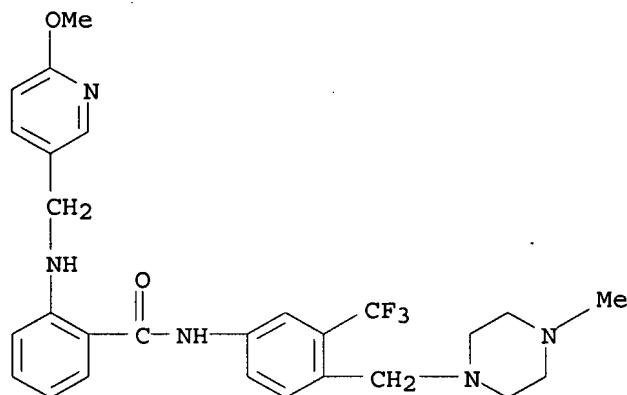


PAGE 2-A



RN 709045-28-3 HCAPLUS

CN Benzamide, 2-[[[6-methoxy-3-pyridinyl)methyl]amino]-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



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Updated Search

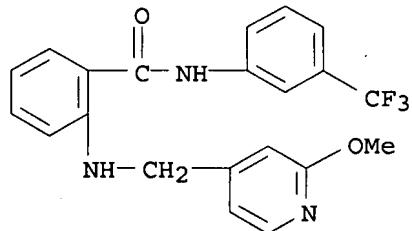
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 709045-71-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of anthranilic acid amide derivs. as neoplastic inhibitors)

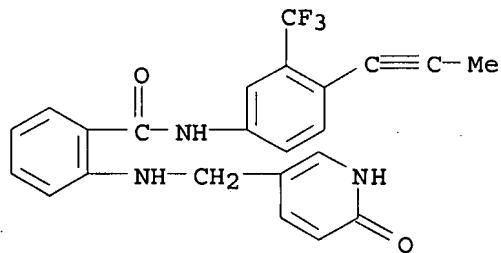
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CN Benzamide, 2-[[[2-methoxy-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



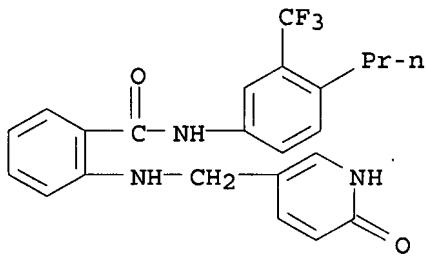
RN 709044-89-3 HCAPLUS

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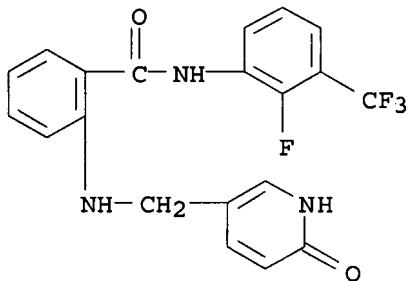
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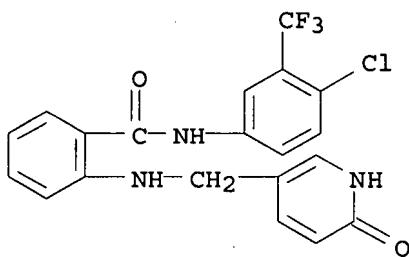
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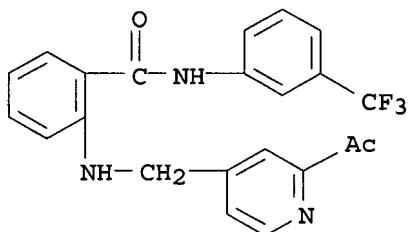
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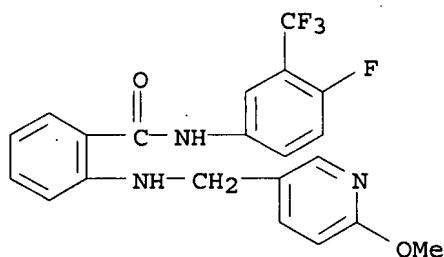
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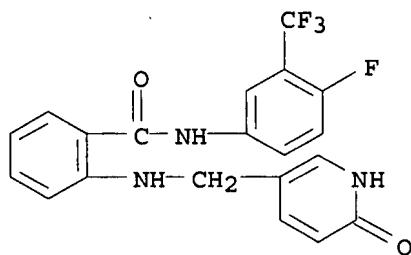
Updated Search

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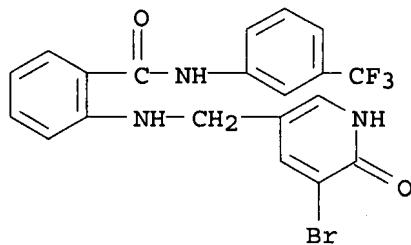
RN 709044-97-3 HCAPLUS

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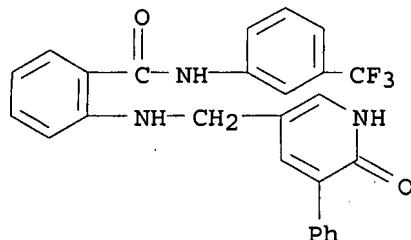
RN 709045-01-2 HCAPLUS

CN Benzamide, 2-[[[(5-bromo-1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

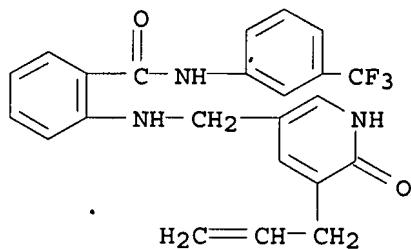


RN 709045-03-4 HCAPLUS

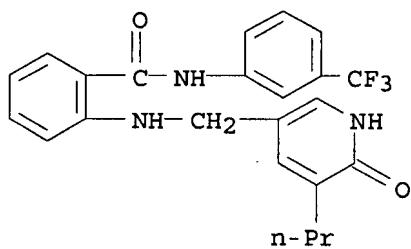
CN Benzamide, 2-[[[(1,6-dihydro-6-oxo-5-phenyl-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



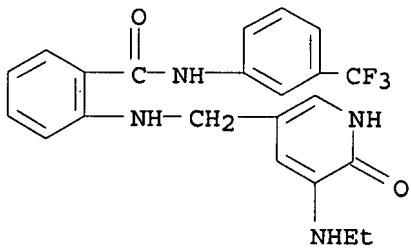
RN 709045-06-7 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-6-oxo-5-(2-propenyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



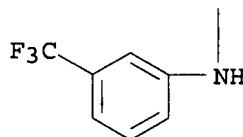
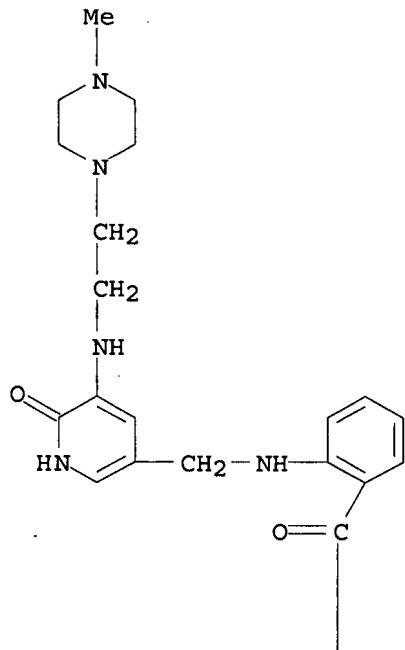
RN 709045-07-8 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-6-oxo-5-propyl-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



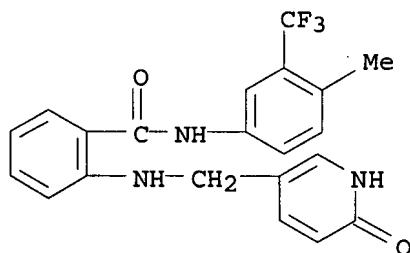
RN 709045-09-0 HCAPLUS
CN Benzamide, 2-[[[5-(ethylamino)-1,6-dihydro-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



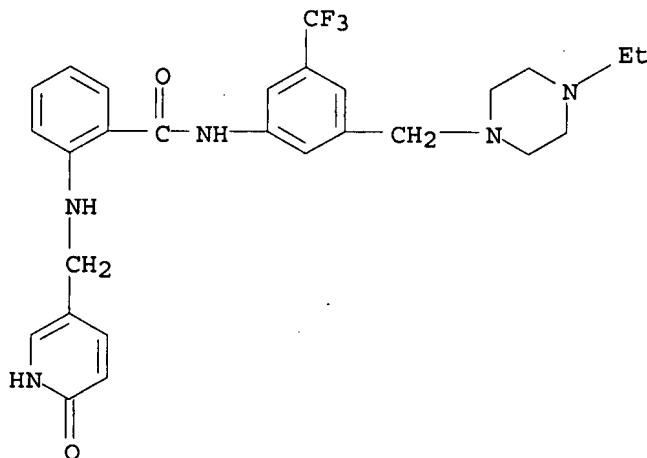
RN 709045-12-5 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-5-[[2-(4-methyl-1-piperazinyl)ethyl]amino]-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



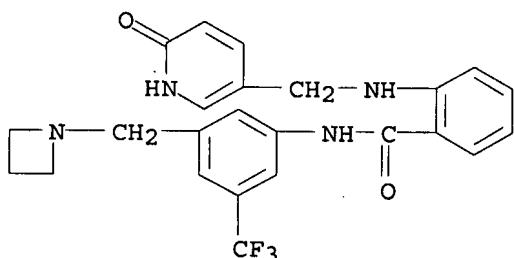
RN 709045-13-6 HCAPLUS
 CN Benzamide, 2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino-N-[4-methyl-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



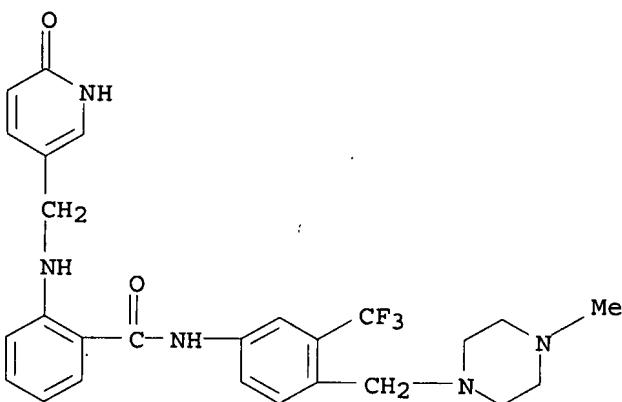
RN 709045-17-0 HCAPLUS
 CN Benzamide, 2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino-N-[3-[(4-ethyl-1-piperazinyl)methyl]-5-(trifluoromethyl)phenyl]- (CA INDEX NAME)



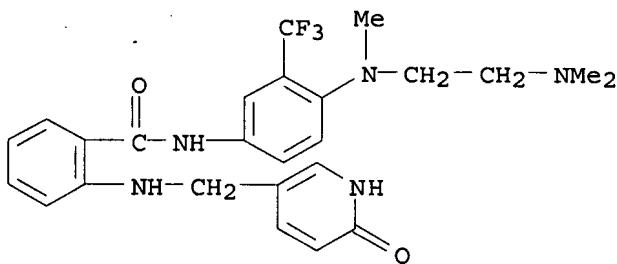
RN 709045-21-6 HCPLUS
 CN Benzamide, N-[3-(1-azetidinylmethyl)-5-(trifluoromethyl)phenyl]-2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]- (CA INDEX NAME)



RN 709045-32-9 HCPLUS
 CN Benzamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

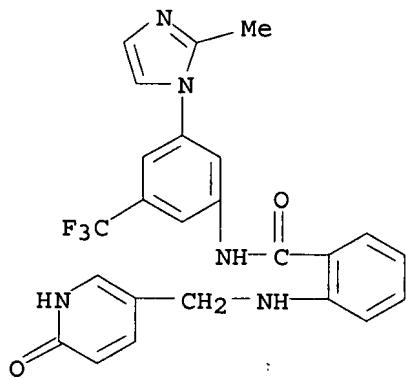


RN 709045-33-0 HCPLUS
 CN Benzamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[[4-[(2-(dimethylamino)ethyl)methyl]amino]-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



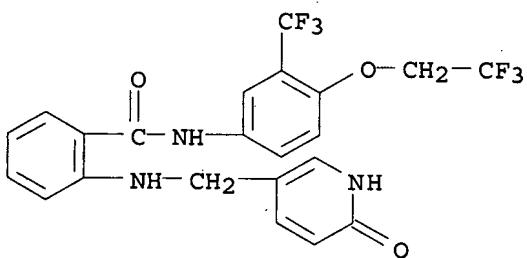
RN 709045-34-1 HCAPLUS

CN Benzamide, 2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino-N-[3-(2-methyl-1H-imidazol-1-yl)-5-(trifluoromethyl)phenyl]- (CA INDEX NAME)



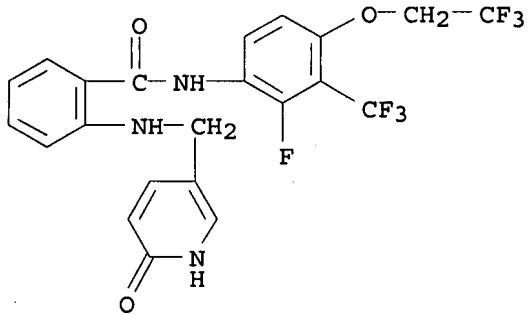
RN 709045-37-4 HCAPLUS

CN Benzamide, 2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino-N-[4-(2,2,2-trifluoroethoxy)-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



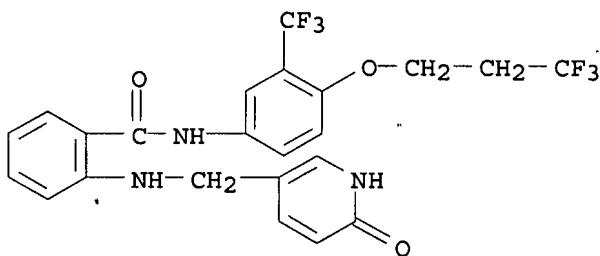
RN 709045-38-5 HCAPLUS

CN Benzamide, 2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino-N-[2-fluoro-4-(2,2,2-trifluoroethoxy)-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



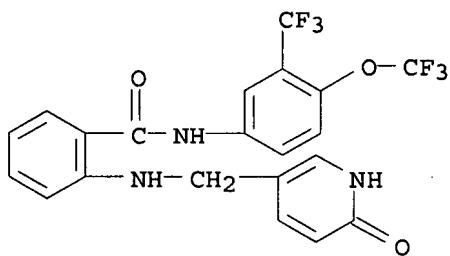
RN 709045-39-6 HCAPLUS

CN Benzamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)-4-(3,3,3-trifluoropropoxy)phenyl]- (CA INDEX NAME)



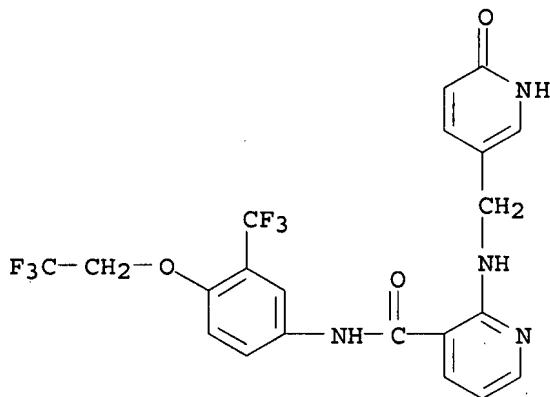
RN 709045-40-9 HCAPLUS

CN Benzamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(trifluoromethoxy)-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

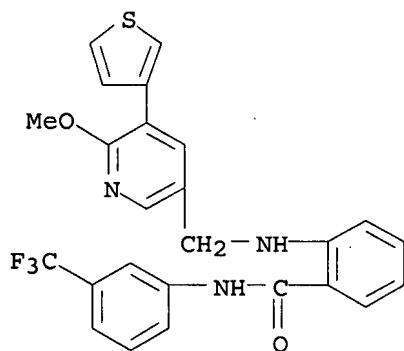


RN 709045-41-0 HCAPLUS

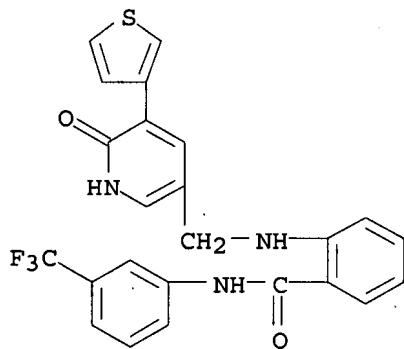
CN 3-Pyridinecarboxamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(2,2,2-trifluoroethoxy)-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



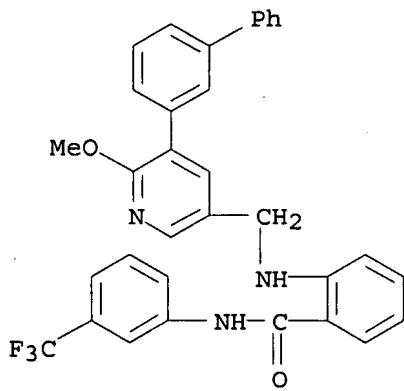
RN 709045-42-1 HCAPLUS
 CN Benzamide, 2-[[[6-methoxy-5-(3-thienyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



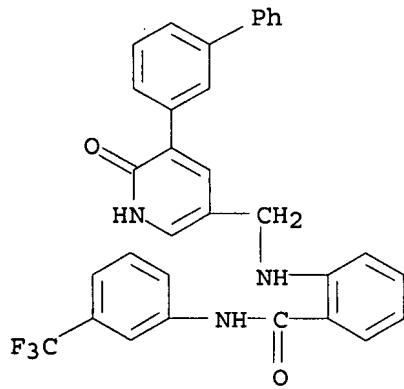
RN 709045-43-2 HCAPLUS
 CN Benzamide, 2-[[[1,6-dihydro-6-oxo-5-(3-thienyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



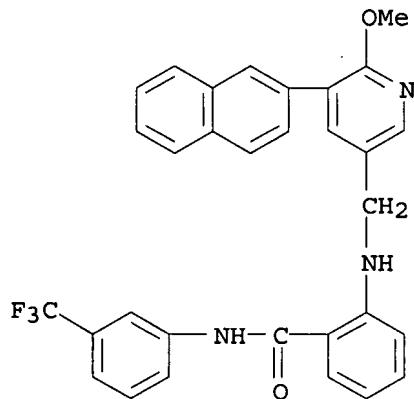
RN 709045-44-3 HCAPLUS
 CN Benzamide, 2-[[[5-[1,1'-biphenyl]-3-yl-6-methoxy-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



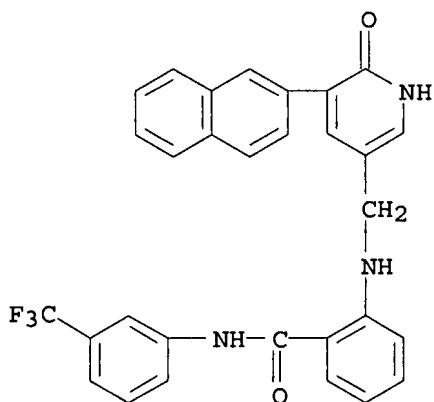
RN 709045-45-4 HCAPLUS
 CN Benzamide, 2-[[[5-[1,1'-biphenyl]-3-yl-1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-46-5 HCAPLUS
 CN Benzamide, 2-[[[6-methoxy-5-(2-naphthalenyl)-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

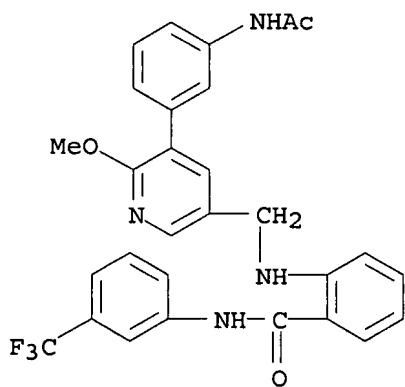


RN 709045-47-6 HCAPLUS
 CN Benzamide, 2-[[[1,6-dihydro-5-(2-naphthalenyl)-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



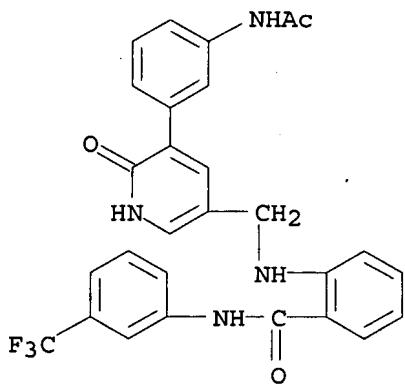
RN 709045-48-7 HCAPLUS

CN Benzamide, 2-[[[5-[3-(acetylamino)phenyl]-6-methoxy-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-49-8 HCAPLUS

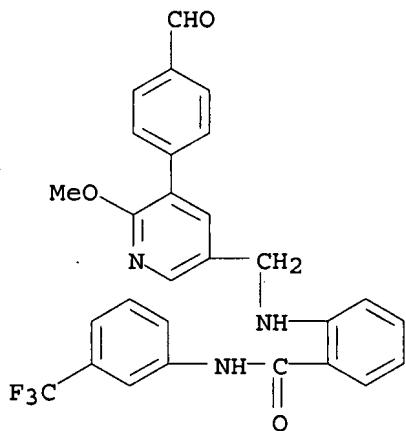
CN Benzamide, 2-[[[5-[3-(acetylamino)phenyl]-1,6-dihydro-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-50-1 HCAPLUS

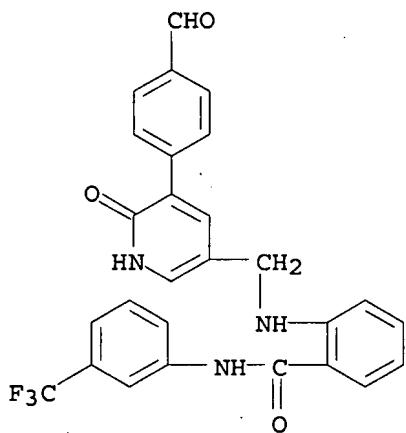
Updated Search

CN Benzamide, 2-[[[5-(4-formylphenyl)-6-methoxy-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



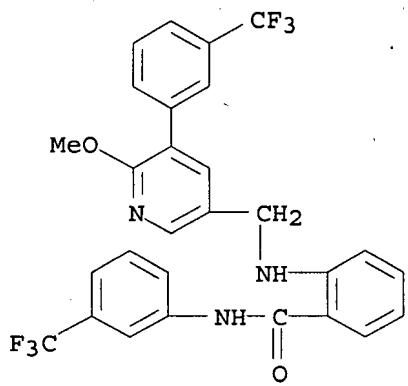
RN 709045-51-2 HCPLUS

CN Benzamide, 2-[[[5-(4-formylphenyl)-1,6-dihydro-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



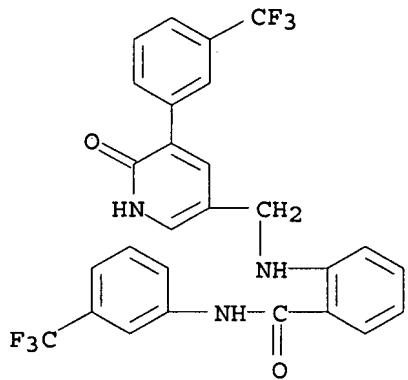
RN 709045-52-3 HCPLUS

CN Benzamide, 2-[[[6-methoxy-5-[3-(trifluoromethyl)phenyl]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



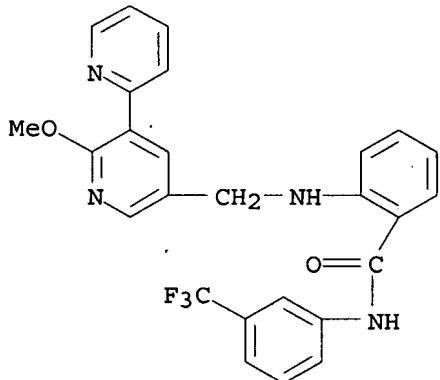
RN 709045-53-4 HCAPLUS

CN Benzamide, 2-[[1,6-dihydro-6-oxo-5-[3-(trifluoromethyl)phenyl]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-54-5 HCAPLUS

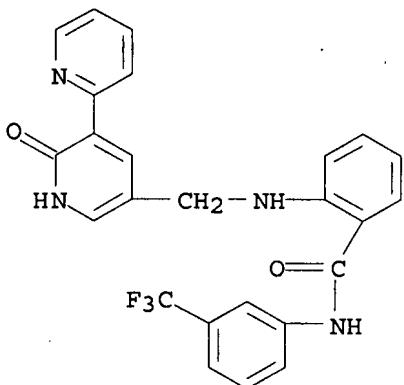
CN Benzamide, 2-[(2'-methoxy[2,3'-bipyridin]-5'-yl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-55-6 HCAPLUS

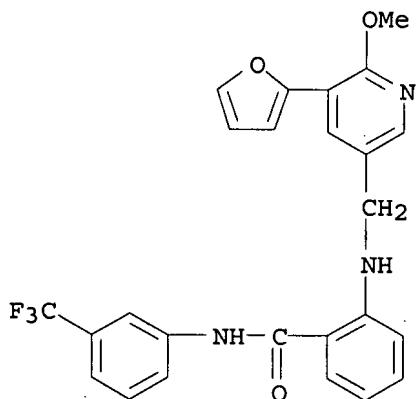
CN Benzamide, 2-[(1',2'-dihydro-2'-oxo[2,3'-bipyridin]-5'-yl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

Updated Search



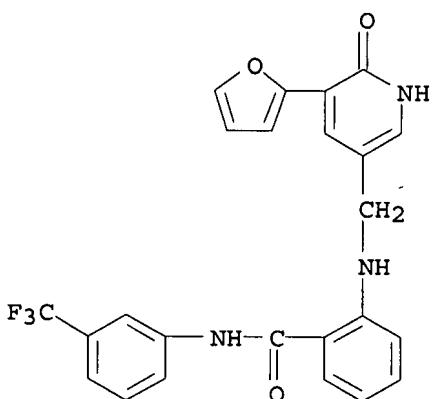
RN 709045-56-7 HCAPLUS

CN Benzamide, 2-[[[5-(2-furanyl)-6-methoxy-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



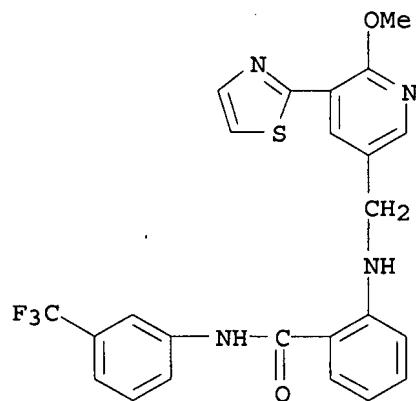
RN 709045-57-8 HCAPLUS

CN Benzamide, 2-[[[5-(2-furanyl)-1,6-dihydro-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



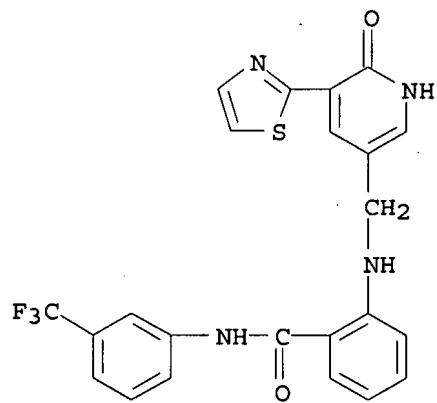
RN 709045-58-9 HCAPLUS

CN Benzamide, 2-[[[6-methoxy-5-(2-thiazolyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



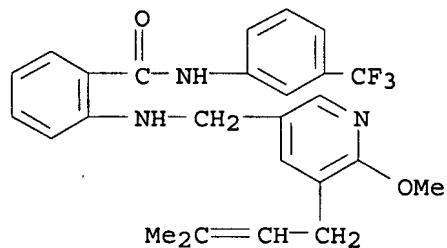
RN 709045-59-0 HCAPLUS

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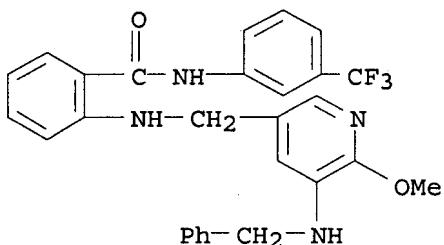
RN 709045-60-3 HCAPLUS

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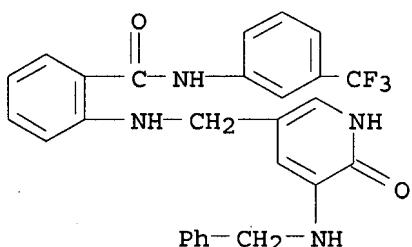
RN 709045-61-4 HCAPLUS

CN Benzamide, 2-[[6-methoxy-5-[(phenylmethyl)amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



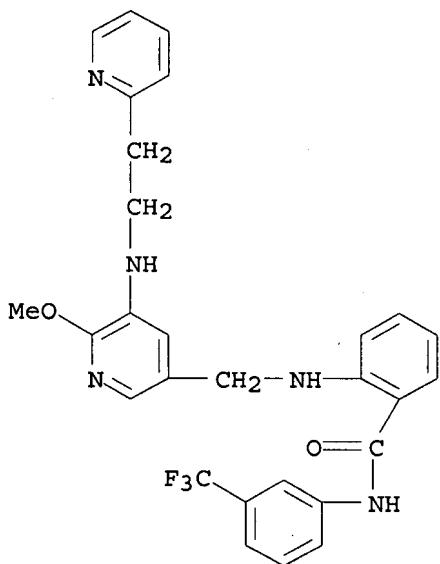
RN 709045-62-5 HCAPLUS

CN Benzamide, 2-[[1,6-dihydro-6-oxo-5-[(phenylmethyl)amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



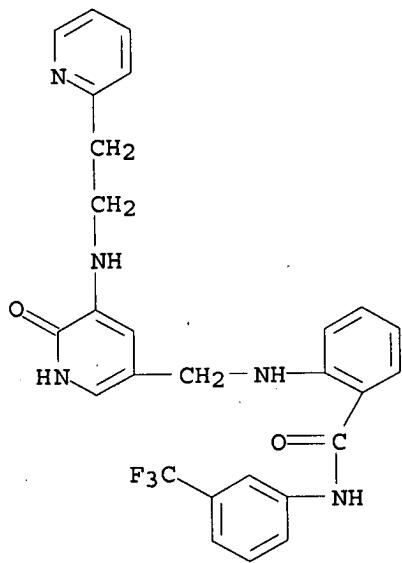
RN 709045-63-6 HCAPLUS

CN Benzamide, 2-[[6-methoxy-5-[[2-(2-pyridinyl)ethyl]amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

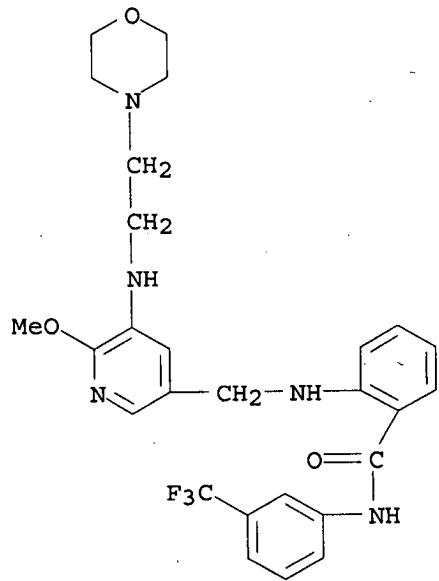


RN 709045-64-7 HCAPLUS

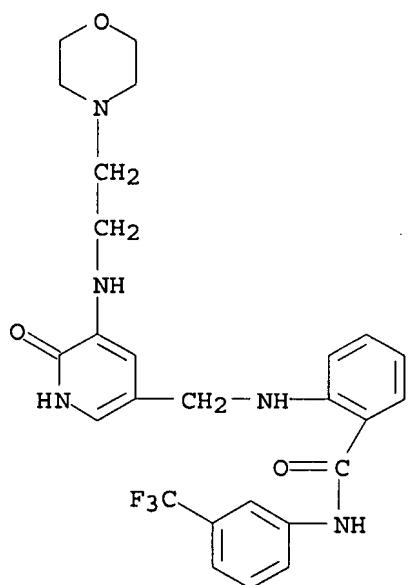
CN Benzamide, 2-[[1,6-dihydro-6-oxo-5-[[2-(2-pyridinyl)ethyl]amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-65-8 HCAPLUS
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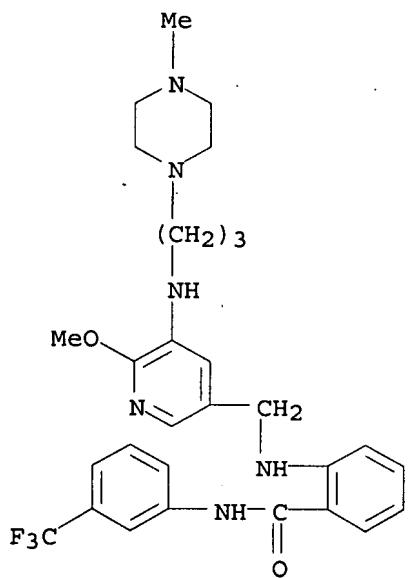


RN 709045-66-9 HCAPLUS
 CN Benzamide, 2-[[[1,6-dihydro-5-[[2-(4-morpholinyl)ethyl]amino]-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



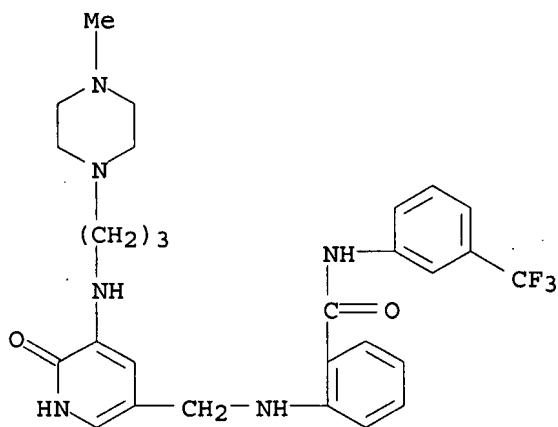
RN 709045-67-0 HCAPLUS

CN Benzamide, 2-[[[6-methoxy-5-[[3-(4-methyl-1-piperazinyl)propyl]amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-68-1 HCAPLUS

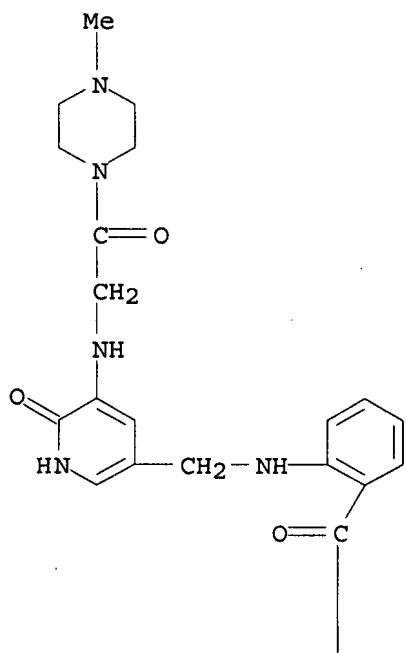
CN Benzamide, 2-[[[1,6-dihydro-5-[[3-(4-methyl-1-piperazinyl)propyl]amino]-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



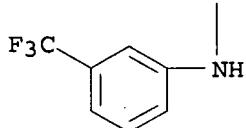
RN 709045-69-2 HCAPLUS

CN Benzamide, 2-[[[1,6-dihydro-5-[[2-(4-methyl-1-piperazinyl)-2-oxoethyl]amino]-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

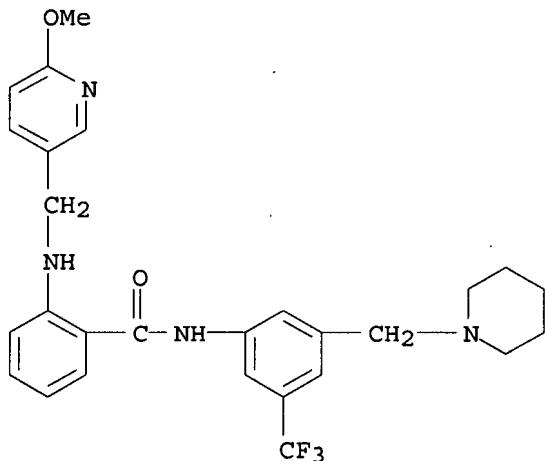
PAGE 1-A



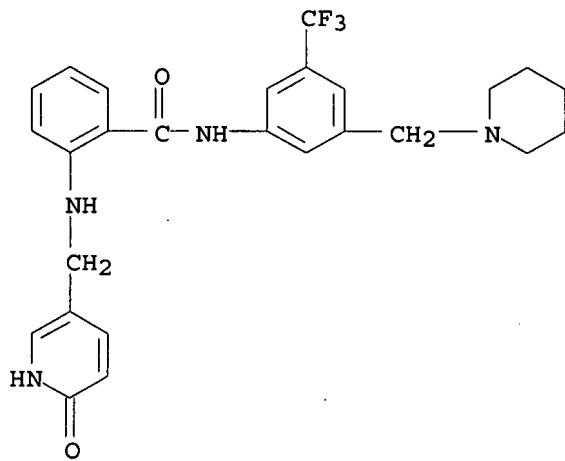
PAGE 2-A



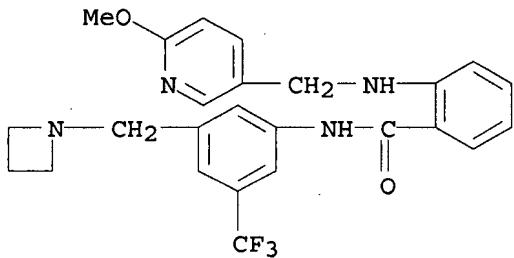
RN 709045-70-5 HCAPLUS
CN Benzamide, 2-[[[(6-methoxy-3-pyridinyl)methyl]amino]-N-[3-(1-piperidinylmethyl)-5-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-71-6 HCAPLUS
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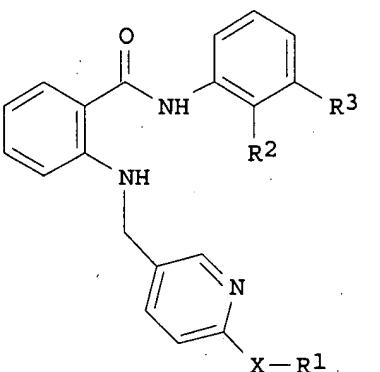


IT 709045-22-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of anthranilic acid amide derivs. as neoplastic inhibitors)
RN 709045-22-7 HCAPLUS
CN Benzamide, N-[3-(1-azetidinylmethyl)-5-(trifluoromethyl)phenyl]-2-[[[(6-methoxy-3-pyridinyl)methyl]amino]- (CA INDEX NAME)



L6 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:376825 HCAPLUS
 DOCUMENT NUMBER: 138:385308
 TITLE: Preparation of anthranilic acid amides and their use as vascular endothelial growth factor receptor tyrosine kinase inhibitors
 INVENTOR(S): Bold, Guido; Furet, Pascal; Manley, Paul William
 PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040102	A1	20030515	WO 2002-EP12444	20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
TW 260222	B	20060821	TW 2002-91132669	20021106
CA 2463968	A1	20030515	CA 2002-2463968	20021107
AU 2002351909	A1	20030519	AU 2002-351909	20021107
AU 2002351909	B2	20070426		
EP 1446382	A1	20040818	EP 2002-787595	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002013970	A	20040831	BR 2002-13970	20021107
CN 1585750	A	20050223	CN 2002-822209	20021107
JP 2005511602	T	20050428	JP 2003-542148	20021107
NZ 532590	A	20051223	NZ 2002-532590	20021107
ZA 2004002940	A	20050210	ZA 2004-2940	20040419
US 2005096356	A1	20050505	US 2004-494591	20040505
US 7091224	B2	20060815		
IN 2004CN00972	A	20060203	IN 2004-CN972	20040506
NO 2004002187	A	20040526	NO 2004-2187	20040526
US 2006178409	A1	20060810	US 2006-374720	20060314
PRIORITY APPLN. INFO.:			GB 2001-26902	A 20011108
			WO 2002-EP12444	W 20021107
OTHER SOURCE(S): GI			US 2004-494591	A1 20040505



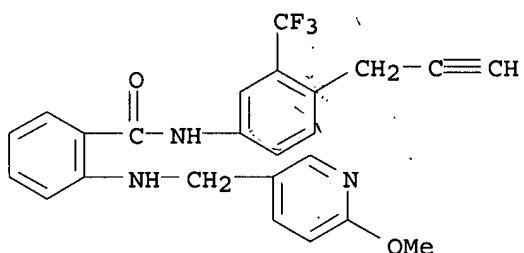
AB Anthranilic acid amide derivs. [I; R1, R2 = H, lower alkyl; R3 = lower perfluoroalkyl; X = O, S; e.g., 2-[(6-Methoxy-3-pyridinyl)methyl]amino-N-[3-(trifluoromethyl)phenyl]benzamide hydrochloride, m.p. 133-135°], which are vascular endothelial growth factor receptor tyrosine kinase inhibitors for the treatment of neoplastic disease, of retinopathy or age-related macular degeneration, are prepared and a I-containing formulation presented (e.g., a soft capsule).

IT 524941-34-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(in the preparation of anthranilic acid amides)

RN 524941-34-2 HCPLUS

CN Benzamide, 2-[[[6-methoxy-3-pyridinyl)methyl]amino]-N-[4-(2-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

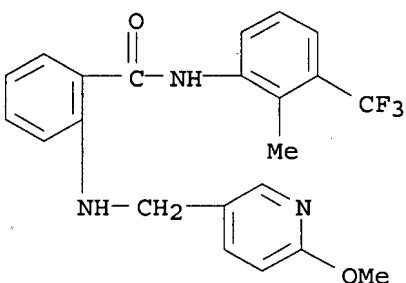


IT 524941-29-5P

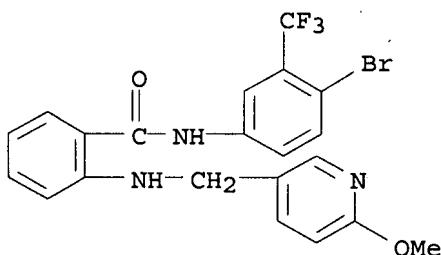
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in the preparation of anthranilic acid amides for use as vascular endothelial growth factor receptor tyrosine kinase inhibitors)

RN 524941-29-5 HCPLUS

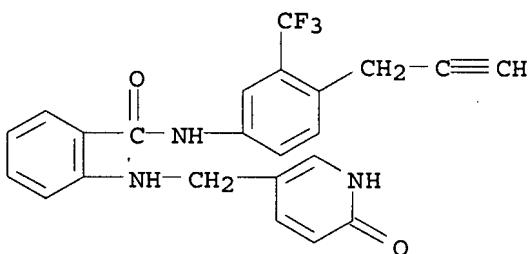
CN Benzamide, 2-[[[6-methoxy-3-pyridinyl)methyl]amino]-N-[2-methyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



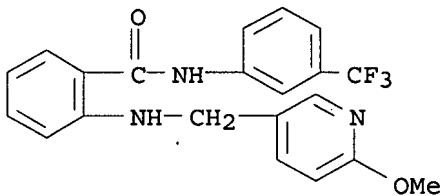
IT 524728-97-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of)
 RN 524728-97-0 HCAPLUS
 CN Benzamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[(6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



IT 524941-33-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 524941-33-1 HCAPLUS
 CN Benzamide, 2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(2-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

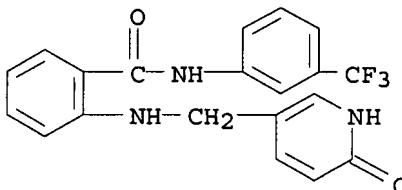


IT 524941-28-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)
 (preparation of anthranilic acid amides and their use as vascular
 endothelial growth factor receptor tyrosine kinase inhibitors)
 RN 524941-28-4 HCAPLUS
 CN Benzamide, 2-[(6-methoxy-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

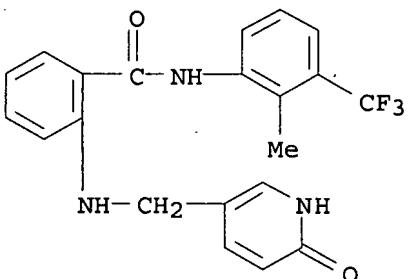


● HCl

IT 524941-35-3P 524941-36-4P
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of anthranilic acid amides and their use as vascular endothelial growth factor receptor tyrosine kinase inhibitors)
 RN 524941-35-3 HCPLUS
 CN Benzamide, 2-[[1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 524941-36-4 HCPLUS
 CN Benzamide, 2-[[1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[2-methyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



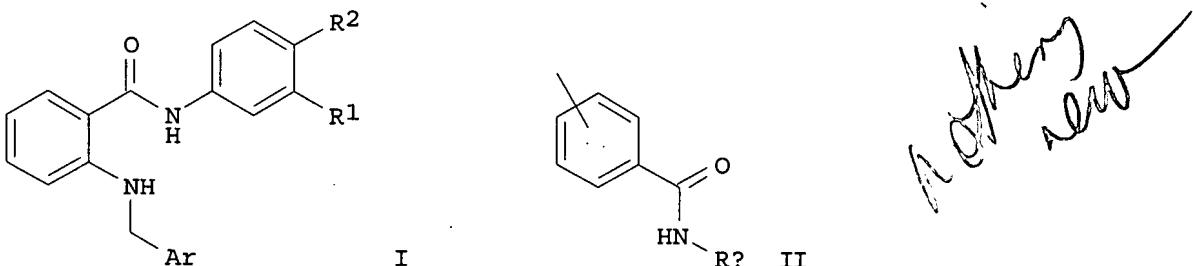
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 5 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:376824 HCPLUS
 DOCUMENT NUMBER: 138:368777
 TITLE: Preparation of pyridyl-substituted anthranilic acid amides for treating neoplastic disease
 INVENTOR(S): Bold, Guido; Furet, Pascal; Manley, Paul
 William
 PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma Gmbh

SOURCE: PCT Int. Appl., 33 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040101	A1	20030515	WO 2002-EP12445	20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
TW 260985	B	20060901	TW 2002-91132668	20021106
CA 2462390	A1	20030515	CA 2002-2462390	20021107
AU 2002342889	A1	20030519	AU 2002-342889	20021107
AU 2002342889	B2	20070301		
EP 1446381	A1	20040818	EP 2002-779536	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002013939	A	20040831	BR 2002-13939	20021107
CN 1578768	A	20050209	CN 2002-821430	20021107
JP 2005508382	T	20050331	JP 2003-542147	20021107
NZ 532587	A	20060224	NZ 2002-532587	20021107
NZ 543915	A	20070629	NZ 2002-543915	20021107
US 2004248947	A1	20041209	US 2004-494222	20040503
US 7067543	B2	20060627		
IN 2004CN00973	A	20060203	IN 2004-CN973	20040506
MX 2004PA04390	A	20050516	MX 2004-PA4390	20040507
NO 2004002137	A	20040525	NO 2004-2137	20040525
ZA 200402623	A	20060531	ZA 2004-2623	20060328
PRIORITY APPLN. INFO.:			GB 2001-26901	A 20011108
			GB 2002-12917	A 20020605
			NZ 2002-532587	A3 20021107
			WO 2002-EP12445	W 20021107

OTHER SOURCE(S): MARPAT 138:368777
 GI



AB The title compds. [I; Ar = II (wherein Ra = H, alkyl; and R1 = H, perfluoroalkyl; R2 = H, halo, alkyl, alkenyl, alkynyl); or Ar = 4-pyridyl and R1 = perfluoroalkyl; R2 = Br, I, alkyl, alkenyl, alkynyl; or R1 = H, and R2 = F, Br, I, Et, alkyl, alkenyl or alkynyl] and their N-oxides and salts, useful for the treatment especially of a neoplastic disease, such as a

tumor disease, of retinopathy or age-related macular degeneration in the human or animal body, were prepared and formulated. Thus, reductive amination of 4-pyridinecarboxaldehyde with 2-amino-N-(4-bromo-3-trifluoromethylphenyl)benzamide (preparation given) in the presence of NaBH₃CN afforded I [Ar = 4-pyridyl; R₁ = CF₃; R₂ = Br]. The IC₅₀-values that can be found for the compds. I are in range of 0.001 to 1 μM in test for activity against VEGF-receptor tyrosine kinase.

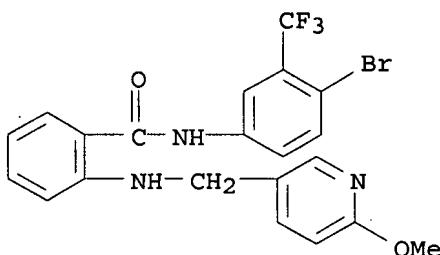
IT 524728-97-0P 524729-01-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyridyl-substituted anthranilic acid amides for treating neoplastic disease)

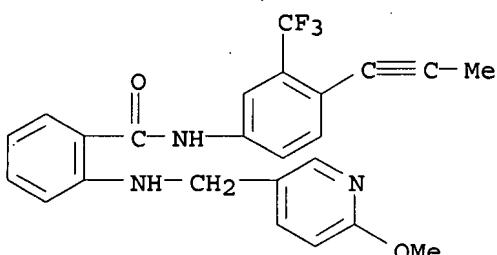
RN 524728-97-0 HCAPLUS

CN Benzamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[(6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 524729-01-9 HCAPLUS

CN Benzamide, 2-[(6-methoxy-3-pyridinyl)methyl]amino]-N-[4-(1-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

1

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:565010 HCAPLUS

DOCUMENT NUMBER: 135:137407

TITLE: Preparation of 2-aminonicotinamides as VEGF-receptor tyrosine kinase inhibitors

INVENTOR(S): Manley, Paul William; Bold, Guido

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.

SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

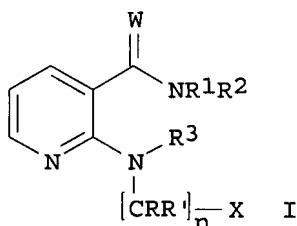
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055114	A1	20010802	WO 2001-EP835	20010125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2396590	A1	20010802	CA 2001-2396590	20010125
AU 200128499	A	20010807	AU 2001-28499	20010125
AU 771626	B2	20040401		
BR 2001007805	A	20021022	BR 2001-7805	20010125
EP 1259487	A1	20021127	EP 2001-946854	20010125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200204083	A2	20030328	HU 2002-4083	20010125
JP 2003520853	T	20030708	JP 2001-555056	20010125
JP 3894793	B2	20070322		
NZ 520005	A	20040227	NZ 2001-520005	20010125
RU 2296124	C2	20070327	RU 2002-121645	20010125
NO 2002003218	A	20020916	NO 2002-3218	20020702
NO 323826	B1	20070709		
US 2003032656	A1	20030213	US 2002-181005	20020711
US 6624174	B2	20030923		
MX 2002PA07319	A	20021129	MX 2002-PA7319	20020726
ZA 2002005988	A	20030728	ZA 2002-5988	20020726
HK 1050895	A1	20051230	HK 2003-103030	20030429
PRIORITY APPLN. INFO.:			GB 2000-1930	A 20000127
			WO 2001-EP835	W 20010125

OTHER SOURCE(S): MARPAT 135:137407
GI

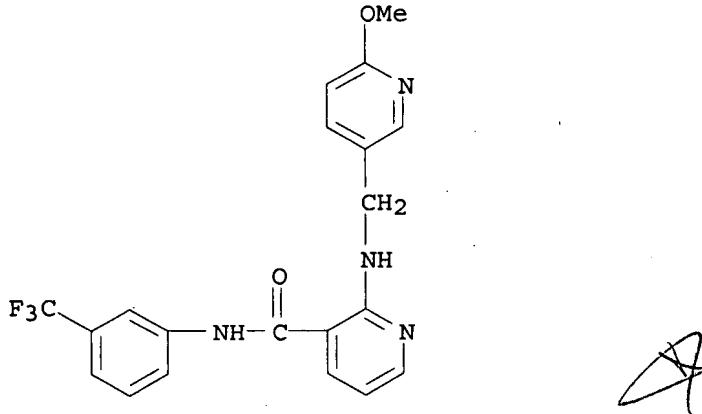


AB The title compds. [I; n = 1-6; W = O, S; R1, R3 = H, alkyl, acyl; R2 = (un)substituted cycloalkyl, aryl, mono- or bicyclic heteroaryl comprising one or more ring N atoms and 0-2 heteroatoms selected from O and S; R, R' = H, alkyl; X = (un)substituted aryl, mono- or bicyclic heteroaryl comprising one or more ring N atoms and 0-2 heteroatoms selected from O and S] and their pharmaceutically acceptable salts, useful for therapy of a disease which responds to an inhibition of the VEGF-receptor tyrosine kinase activity (such as neoplastic disease), were prepared and formulated. Thus, amidation of 3-aminobenzotrifluoride with 2-chloronicotinoyl chloride followed by reacting 4-pyridineethanamine with the resulting carboxamide afforded I [n = 2; R, R' = H; X = 4-pyridyl; W = O; R1, R3 = H; R2 = 3-(F3C)C6H4].

IT 352227-59-9P 352227-60-2P 352227-82-8P
352227-83-9P 352227-84-0P 352227-88-4P
352227-93-1P 352227-97-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-aminonicotinamides as VEGF-receptor tyrosine kinase inhibitors)

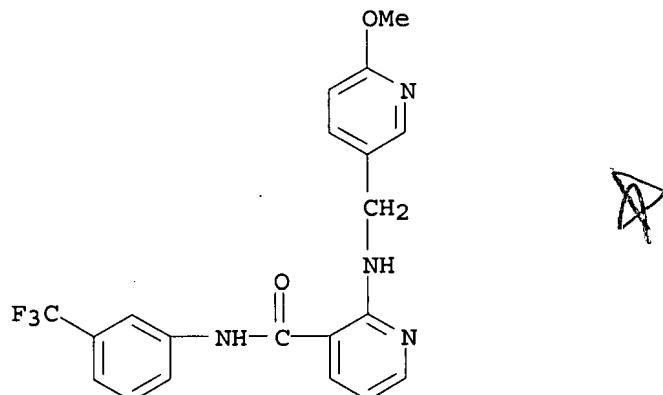
RN 352227-59-9 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[[(6-methoxy-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 352227-60-2 HCAPLUS

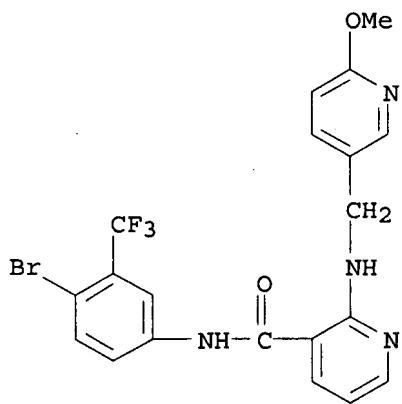
CN 3-Pyridinecarboxamide, 2-[[[(6-methoxy-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

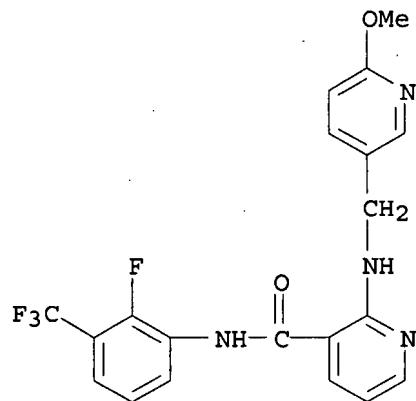
RN 352227-82-8 HCAPLUS

CN 3-Pyridinecarboxamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[[[(6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



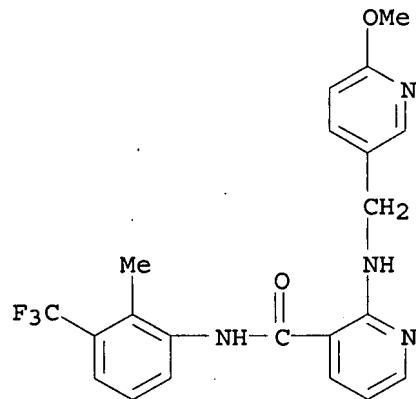
RN 352227-83-9 HCPLUS

CN 3-Pyridinecarboxamide, N-[2-fluoro-3-(trifluoromethyl)phenyl]-2-[[[(6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



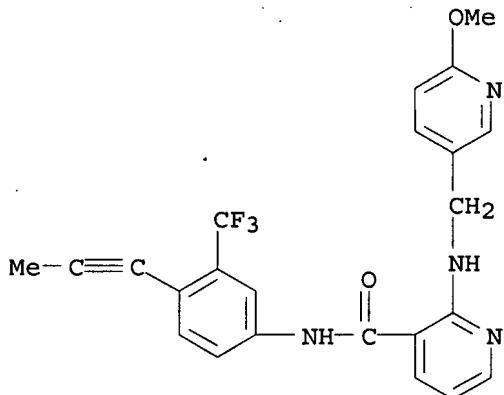
RN 352227-84-0 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[[(6-methoxy-3-pyridinyl)methyl]amino]-N-[2-methyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



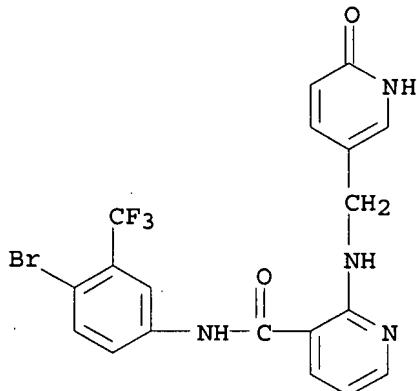
RN 352227-88-4 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[[(6-methoxy-3-pyridinyl)methyl]amino]-N-[4-(1-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



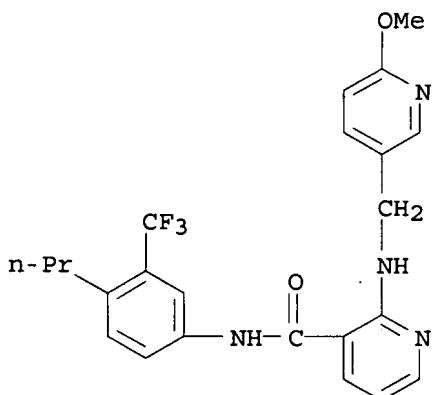
RN 352227-93-1 HCAPLUS

CN 3-Pyridinecarboxamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 352227-97-5 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[(6-methoxy-3-pyridinyl)methyl]amino]-N-[4-propyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



IT 352227-58-8P 352227-90-8P 352227-91-9P

Updated Search

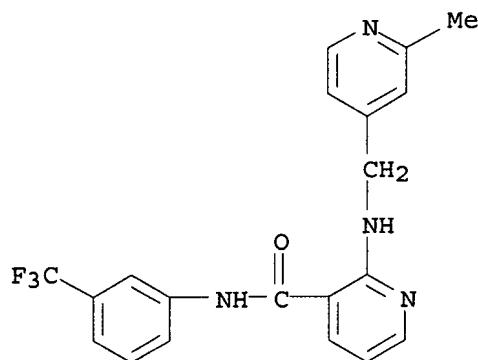
352227-94-2P 352227-95-3P 352227-96-4P

352228-08-1P 352228-09-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aminonicotinamides as VEGF-receptor tyrosine kinase inhibitors)

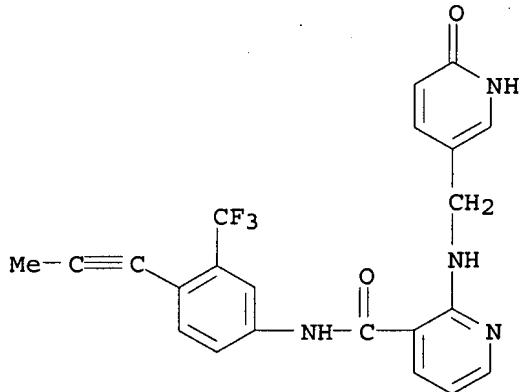
RN 352227-58-8 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-methyl-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



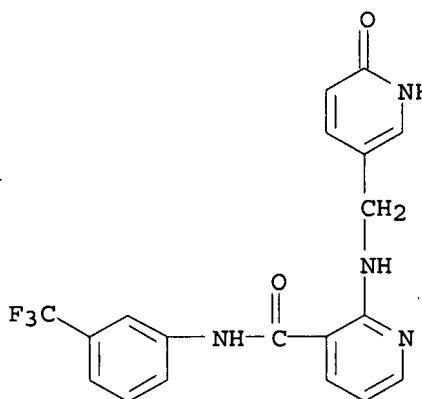
RN 352227-90-8 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[[1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(1-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



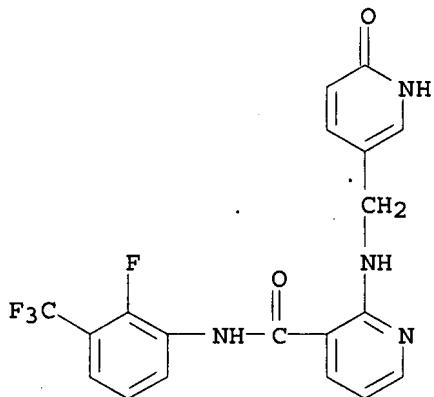
RN 352227-91-9 HCAPLUS

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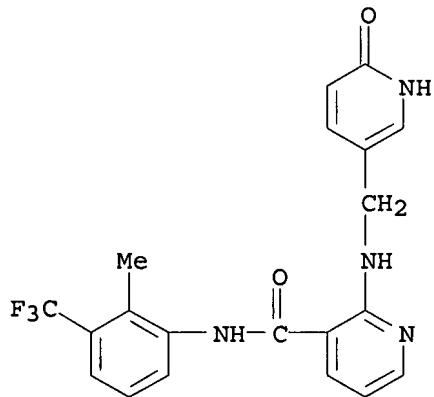
RN 352227-94-2 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[2-fluoro-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



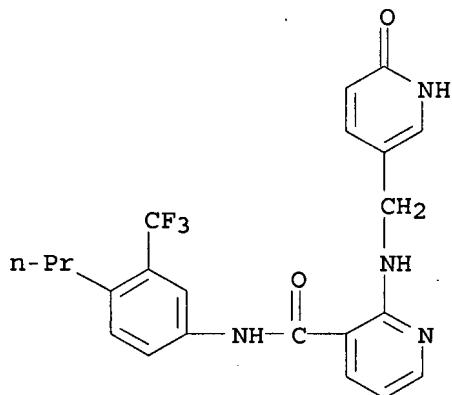
RN 352227-95-3 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[2-methyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



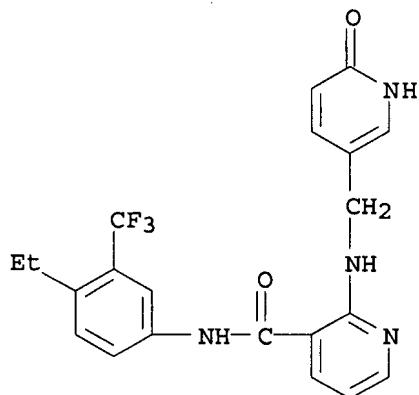
RN 352227-96-4 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-propyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



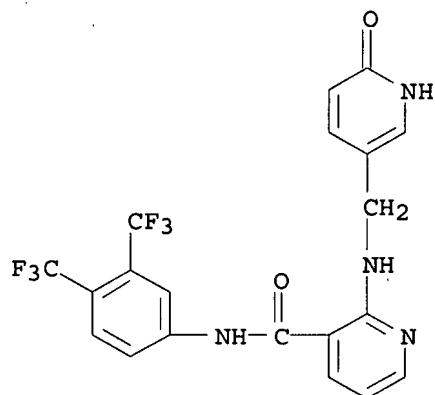
RN 352228-08-1 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-ethyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 352228-09-2 HCAPLUS

CN 3-Pyridinecarboxamide, N-[3,4-bis(trifluoromethyl)phenyl]-2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

Updated Search

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:335388 HCAPLUS
 DOCUMENT NUMBER: 132:347491
 TITLE: Preparation of N-aryl(thio)anthranilic acid amides as VEGF receptor tyrosine kinase inhibitors
 INVENTOR(S): Altmann, Karl-Heinz; Bold, Guido; Furet, Pascal; Manley, Paul William; Wood, Jeanette Marjorie; Ferrari, Stefano; Hofmann, Francesco; Mestan, Jurgen; Huth, Andreas; Kruger, Martin; Seidelmann, Dieter; Menrad, Andreas; Haberey, Martin; Thierauch, Karl-Heinz
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Schering Aktiengesellschaft
 SOURCE: PCT Int. Appl., 77 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

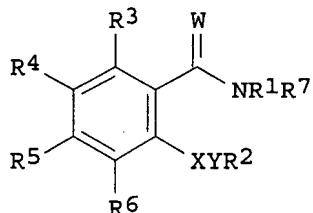
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027820	A1	20000518	WO 1999-EP8545	19991108
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2346898	A1	20000518	CA 1999-2346898	19991108
BR 9915210	A	20010724	BR 1999-15210	19991108
TR 200101237	T2	20010821	TR 2001-200101237	19991108
EP 1129075	A1	20010905	EP 1999-971802	19991108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 200104188	A2	20020328	HU 2001-4188	19991108
JP 2002529453	T	20020910	JP 2000-581000	19991108
AU 758230	B2	20030320	AU 2000-13811	19991108
NZ 511339	A	20030725	NZ 1999-511339	19991108
RU 2286338	C2	20061027	RU 2001-114978	19991108
NO 2001001894	A	20010704	NO 2001-1894	20010417
ZA 2001003290	A	20030123	ZA 2001-3290	20010423
MX 2001PA04256	A	20030606	MX 2001-PA4256	20010427
US 2002019414	A1	20020214	US 2001-850434	20010507
US 6448277	B2	20020910		
IN 2001CN00638	A	20050304	IN 2001-CN638	20010508
ZA 2001004673	A	20020909	ZA 2001-4673	20010607
US 2003064992	A1	20030403	US 2002-180289	20020626
US 6878720	B2	20050412		
US 2004198782	A1	20041007	US 2004-828951	20040421
US 7002022	B2	20060221		
US 2006074112	A1	20060406	US 2005-254897	20051020
PRIORITY APPLN. INFO.:			GB 1998-24579	A 19981110
			WO 1999-EP8545	W 19991108
			US 2001-850434	A3 20010507
			US 2002-180289	A3 20020626

OTHER SOURCE(S) :
GI

MARPAT 132:347491

US 2004-828951

A3 20040421



I

AB Use of title compds. I; W = O, S; X = CR9R10(CH2)n, SO2; R9, R10 = H, alkyl; n = 0-3; R1 = aryl; R2 = mono- or bicyclic heteroaryl with the exception that R2 cannot = 2-phthalimidyl, and when Y = SO2 cannot represent 2,1,3-benzothiadiazol-4-yl; R3-R6 = H, substituent; R7, R8 = H, alkyl; or a N-oxide or a pharmaceutically acceptable salt thereof, for the preparation of a pharmaceutical product for the treatment of a neoplastic disease which responds to an inhibition of the VEGF receptor tyrosine kinase activity is claimed. Thus, a mixture of 4-pyridinecarboxaldehyde and 2-amino-N-(4-trifluoromethylphenyl)benzamide (preparation given) in MeOH containing

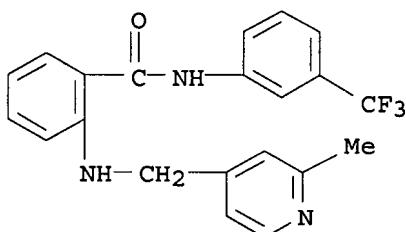
HOAc was treated with NaBH3CN followed by 16 h stirring to give 2-[(4-pyridyl)methyl]amino-N-[4-(trifluoromethyl)phenyl]benzamide. Tested I inhibited Flt-1 VEGF receptor tyrosine kinase with IC50 = 0.18-0.56 μM.

IT 269391-00-6P 269391-01-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-aryl(thio)anthranilic acid amides as VEGF receptor tyrosine kinase inhibitors)

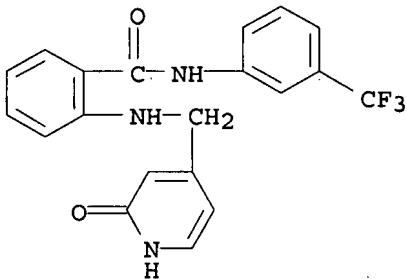
RN 269391-00-6 HCAPLUS

CN Benzamide, 2-[[2-methyl-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 269391-01-7 HCAPLUS

CN Benzamide, 2-[[1,2-dihydro-2-oxo-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 16:47:58 ON 01 OCT 2007)

FILE 'REGISTRY' ENTERED AT 16:48:04 ON 01 OCT 2007

L1 STRUCTURE uploaded
 L2 STRUCTURE uploaded
 L3 8 S L2
 L4 207 S L2 FULL

FILE 'HCAPLUS' ENTERED AT 16:54:00 ON 01 OCT 2007

L5 16 S L4
 L6 5 S L5 AND BOLD, G?/AU

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 L7 11 L5 NOT L6

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 154 FURET, P?/AU
 L8 1 L7 AND FURET, P?/AU

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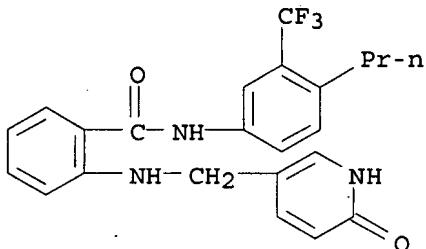
L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:1309915 HCAPLUS
 DOCUMENT NUMBER: 147:180753
 TITLE: Structural biology contributions to the discovery of drugs to treat chronic myelogenous leukemia
 AUTHOR(S): Cowan-Jacob, Sandra W.; Fendrich, Gabriele; Floersheimer, Andreas; Furet, Pascal; Liebetanz, Janis; Rummel, Gabriele; Rheinberger, Paul; Centeleghe, Mario; Fabbro, Dorian; Manley, Paul W.
 CORPORATE SOURCE: Novartis Institutes for Biomedical Research, Basel, Switz.
 SOURCE: Acta Crystallographica, Section D: Biological Crystallography (2007), D63(1), 80-93
 CODEN: ABCRE6; ISSN: 0907-4449
 PUBLISHER: Blackwell Publishing Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Chronic myelogenous leukemia (CML) results from the Bcr-Abl oncprotein, which has a constitutively activated Abl tyrosine kinase domain. Although most chronic phase CML patients treated with imatinib as first-line therapy maintain excellent durable responses, patients who have progressed to advanced-stage CML frequently fail to respond or lose their response to

therapy owing to the emergence of drug-resistant mutants of the protein. More than 40 such point mutations have been observed in imatinib-resistant patients. The crystal structures of wild-type and mutant Abl kinase in complex with imatinib and other small-mol. Abl inhibitors were determined, with the aim of understanding the mol. basis of resistance and to aid in the design and optimization of inhibitors active against the resistance mutants. These results are presented in a way which illustrates the approaches used to generate multiple structures, the type of information that can be gained and the way that this information is used to support drug discovery.

IT 709044-90-6, NVP-AEG 082
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (structural biol. contributions to the discovery of drugs to treat chronic myelogenous leukemia)

RN 709044-90-6 HCAPLUS

CN Benzamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-propyl-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 16:47:58 ON 01 OCT 2007)

FILE 'REGISTRY' ENTERED AT 16:48:04 ON 01 OCT 2007

L1 STRUCTURE uploaded
 L2 STRUCTURE uploaded
 L3 8 S L2
 L4 207 S L2 FULL

FILE 'HCAPLUS' ENTERED AT 16:54:00 ON 01 OCT 2007

L5 16 S L4
 L6 5 S L5 AND BOLD, G?/AU
 L7 11 S L5 NOT L6
 L8 1 S L7 AND FURET, P?/AU

=> s 17 not 18

L9 10 L7 NOT L8

=> s 19 and manley, p?/au

214 MANLEY, P?/AU

L10 0 L9 AND MANLEY, P?/AU

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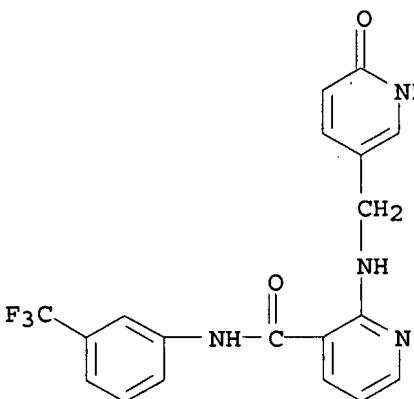
L9 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

Updated Search

ACCESSION NUMBER: 2007:150229 HCAPLUS
 DOCUMENT NUMBER: 146:221063
 TITLE: Method for assaying anti-tumor effect of angiogenesis inhibitor
 INVENTOR(S): Uenaka, Toshimitsu; Yamamoto, Yuji; Matsui, Junji
 PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 147pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007015578	A1	20070208	WO 2006-JP315698	20060802
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			JP 2005-224173	A 20050802
			JP 2006-164700	A 20060614

OTHER SOURCE(S): MARPAT 146:221063
 AB Disclosed is a method for predicting the anti-tumor effect of an angiogenesis inhibitor. The method comprises evaluating the EGF-dependence property of an angiogenesis inhibitor with respect to proliferation and/or survival of tumor cells, and using the evaluated EGF-dependence property as a measure. The anti-tumor effect of an angiogenesis inhibitor correlates with the EGF-dependency property of the inhibitor with respect to proliferation and/or survival of tumor cells. Therefore, an angiogenesis inhibitor is capable of exerting an excellent anti-tumor effect by using it in combination with a substance having an EGF inhibitory effect.
 IT 352227-91-9, ABP 309
 RL: ANT (Analyte); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (method for assaying anti-tumor effect of angiogenesis inhibitor by evaluating EGF-dependency)
 RN 352227-91-9 HCAPLUS
 CN 3-Pyridinecarboxamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:144036 HCAPLUS

DOCUMENT NUMBER: 146:221062

TITLE: Method for predicting antitumor efficacy of angiogenesis inhibitor

INVENTOR(S): Matsui, Junji; Semba, Taro

PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan

SOURCE: PCT Int. Appl., 104pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007015569	A1	20070208	WO 2006-JP315563	20060801
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: JP 2005-223440 A 20050801

OTHER SOURCE(S): MARPAT 146:221062

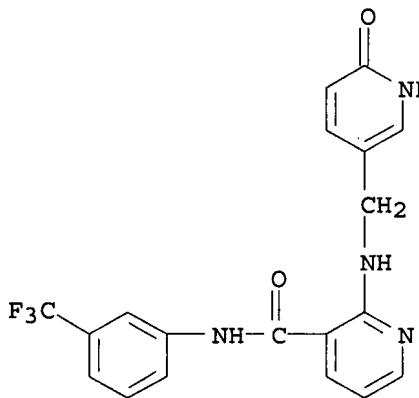
AB A method for predicting the antitumor efficacy of an angiogenesis inhibitor is provided, which comprises measuring the number of blood vessels surrounded by pericytes in tumor, and using the measurement value as a measure for the anti-tumor effect.

IT 352227-91-9

RL: ANT (Analyte); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (method for predicting antitumor efficacy of angiogenesis inhibitor)

RN 352227-91-9 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



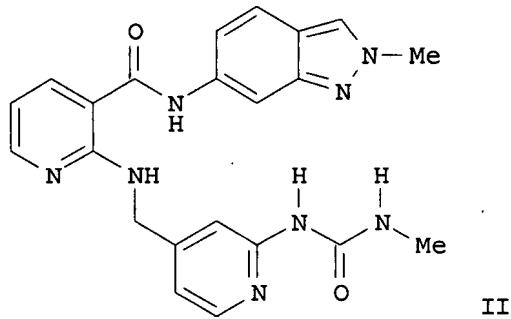
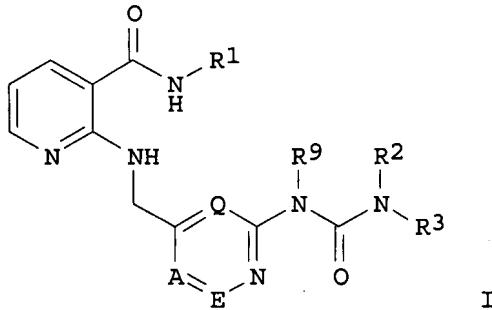
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:440299 HCAPLUS
 DOCUMENT NUMBER: 144:468030
 TITLE: Preparation of novel nicotinamide pyridinureas as vascular endothelial growth factor (VEGF) receptor kinase inhibitors
 INVENTOR(S): Bohlmann, Rolf; Haberey, Martin; Hess-Stumpp, Holger; Huth, Andreas; Ince, Stuart; Krueger, Martin; Thierauch, Karl-Heinz
 PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
 SOURCE: PCT Int. Appl., 58 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006048249	A1	20060511	WO 2005-EP11709	20051028
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1655297	A1	20060510	EP 2004-90420	20041103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
AU 2005300734	A1	20060511	AU 2005-300734	20051028
CA 2586265	A1	20060511	CA 2005-2586265	20051028
EP 1807416	A1	20070718	EP 2005-806225	20051028
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

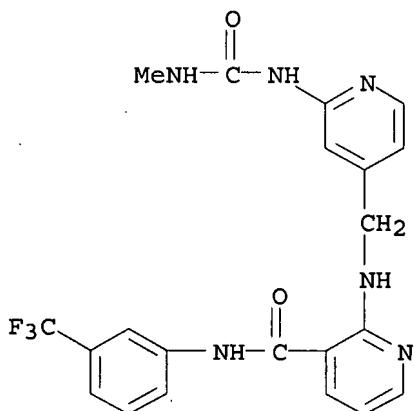
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
 US 2006160861 A1 20060720 US 2005-262953 20051101
 IN 2007DN02886 A 20070817 IN 2007-DN2886 20070418
 PRIORITY APPLN. INFO.: EP 2004-90420 A 20041103
 US 2004-626918P P 20041112
 WO 2005-EP11709 W 20051028

OTHER SOURCE(S): CASREACT 144:468030; MARPAT 144:468030
 GI



- AB** The title compds. I [A, E and Q = CH or N (only maximum of 2 N atoms are contained in the ring); R1 = (un)substituted (hetero)aryl; R2, R3, R9 = H, alkyl, haloalkyl, etc.; or R9 = H, and NR2R3 = (un)substituted 3-8 membered heterocycloalkyl, preferably 4-7 membered heterocycloalkyl, more preferably 5-6 membered heterocycloalkyl; or R3 = H, alkyl, alkoxyalkyl, and R2 and R9 together with the two N atoms to which they are attached form 5-7 membered ring, preferably 5-6 membered ring] which are VEGF receptor kinase inhibitors useful as pharmaceutical agents for preventing or treating diseases that are triggered by persistent angiogenesis, were prepared E.g., a multi-step synthesis of II, starting from 2-chloroisonicotinonitrile, was given. II showed IC50 of 10 nM against KDR kinase (VEGFR-2). Pharmaceutical composition comprising the compound I is disclosed.
- IT** 886586-76-1P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of novel nicotinamide pyridinureas as VEGF receptor kinase inhibitors for treating and preventing diseases that are triggered by persistent angiogenesis)
- RN** 886586-76-1 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[2-[(methylamino)carbonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:268466 HCAPLUS

DOCUMENT NUMBER: 144:324798

TITLE: Simultaneous use of sulfonamide-containing compound and angiogenesis inhibitor

INVENTOR(S): Owa, Takashi; Ozawa, Yoichi; Semba, Taro

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 270 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006030941	A1	20060323	WO 2005-JP17228	20050913
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
WO 2006030947	A1	20060323	WO 2005-JP17238	20050913
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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 KG, KZ, MD, RU, TJ, TM
 US 2006135486 A1 20060622 US 2005-226655 20050913
 EP 1797877 A1 20070620 EP 2005-785820 20050913
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 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
 BA, HR, MK, YU
 PRIORITY APPLN. INFO.: US 2004-609452P P 20040913
 JP 2005-54150 A 20050228
 JP 2005-54475 A 20050228
 WO 2005-JP17238 W 20050913

OTHER SOURCE(S): MARPAT 144:324798

AB A pharmaceutical composition comprising a sulfonamide-containing compound combined

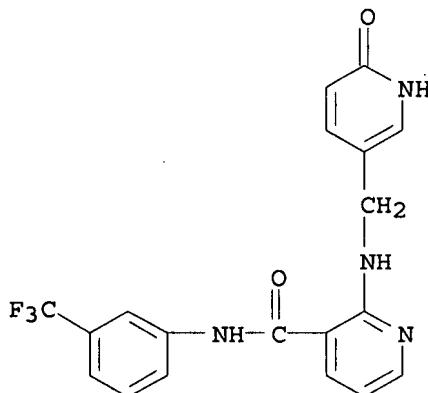
with an angiogenesis inhibitor.

IT 352227-91-9, ABP 309

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (sulfonamide-containing compds. and angiogenesis inhibitors for combination chemotherapy of cancer)

RN 352227-91-9 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:953989 HCAPLUS

DOCUMENT NUMBER: 143:242054

TITLE: Pharmaceutical combination comprising a CDK inhibitor and a VEGF receptor inhibitor

INVENTOR(S): Siemeister, Gerhard

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: Eur. Pat. Appl., 40 pp.

CODEN: EPXXDW

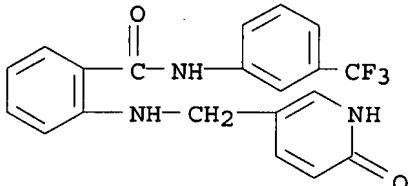
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1568368	A1	20050831	EP 2004-90071	20040226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			EP 2004-90071	20040226
OTHER SOURCE(S):		MARPAT 143:242054		
AB	Pharmaceutical combinations comprising a cyclin-dependent kinase (CDK) inhibitor and a vascular endothelial growth factor receptor (VEGF-R) inhibitor and their use for the treatment of different diseases are described. A CDK inhibitor and a VEGF-R inhibitor are used as a combined preparation simultaneously, sep. or sequentially. For example, a combination of a CDK inhibitor, i.e., N-[5-[[[5-(1,1-dimethylethyl)-2-oxazolyl]methyl]thio]-2-thiazolyl]-4-piperidinecarboxamide and a VEGF-R inhibitor, i.e., (4-chlorophenyl)[4-(4-pyridylmethyl)phthalazin-1-yl]ammonium hydrogen succinate was evaluated in a human estrogen-independent mammary carcinoma model, xenografted in mice. The combination of both compds. at a dosing of 10 mg/kg i.p. once daily for the CDK inhibitor and 50 mg/kg per orally twice daily for the VEGF-R inhibitor showed a clear, synergistic or substantially greater, inhibition of tumor growth in comparison to monotherapy and the control group. The results show that a combination therapy using a CDK inhibitor and VEGF-R inhibitor was substantially superior in the efficacy of tumor growth inhibition as compared to monotherapy with the each of the sep. compds.			
IT	524941-35-3 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combination comprising CDK inhibitor and VEGF receptor inhibitor for treatment or prophylaxis of various diseases)			
RN	524941-35-3 HCPLUS			
CN	Benzamide, 2-[[1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)			

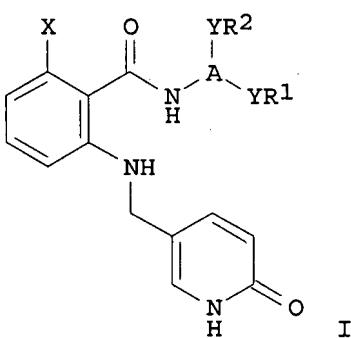


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 10 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:1127340 HCPLUS
 DOCUMENT NUMBER: 142:74461
 TITLE: Preparation of pyridonylmethyl anthranylamides as inhibitors of vascular endothelial growth factor receptors VEGFR-2 and VEGFR-3.
 INVENTOR(S): Huth, Andreas; Krueger, Martin; Zorn, Ludwig; Ince, Stuart; Bohlmann, Rolf; Thierauch, Karl-Heinz; Menrad, Andreas; Haberey, Martin; Hess-Stumpp, Holger
 PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
 SOURCE: PCT Int. Appl., 36 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111005	A1	20041223	WO 2004-EP6236	20040609
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10327719	A1	20050120	DE 2003-10327719	20030613
AU 2004247377	A1	20041223	AU 2004-247377	20040609
CA 2526041	A1	20041223	CA 2004-2526041	20040609
EP 1633713	A1	20060315	EP 2004-739742	20040609
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1805936	A	20060719	CN 2004-80016364	20040609
BR 2004011360	A	20060725	BR 2004-11360	20040609
JP 2006527228	T	20061130	JP 2006-515873	20040609
US 2005049281	A1	20050303	US 2004-866078	20040614
US 7202260	B2	20070410		
IN 2005DN05428	A	20070817	IN 2005-DN5428	20051124
MX 2005PA13586	A	20060309	MX 2005-PA13586	20051213
NO 2006000196	A	20060112	NO 2006-196	20060112
US 2007135489	A1	20070614	US 2007-654643	20070118
PRIORITY APPLN. INFO.:			DE 2003-10327719	A 20030613
			US 2003-482009P	P 20030625
			WO 2004-EP6236	W 20040609
			US 2004-866078	A3 20040614
OTHER SOURCE(S): GI		MARPAT 142:74461		



AB Title compds. (I; A = aryl, heteroaryl; X = H, F; R1, R2 = H, halo, alkyl, alkoxyalkyl, haloalkyl, cycloalkyl, halocycloalkyl; Y = bond, O, S, SO, SO₂), were prepared Thus, 2-[(6-oxo-1,6-dihydropyridin-3-ylmethyl)amino]benzoic acid (preparation given), N-methylmorpholine, 4-trifluoromethoxyaniline, and HATU were stirred 2.5 h in CH₂Cl₂ at room temp and 1.5 h at 100° bath temperature to give 50.1% 2-[(6-oxo-1,6-dihydropyridin-3-ylmethyl)amino]-N-(4-

trifluoromethoxyphenyl)benzamide. The latter inhibited VEGFR II with IC₅₀ = 180 nM. The invention relates to selected anthranylamide pyridones that inhibit VEGFR-2 and VEGFR-3 and to their use as medicaments for treating diseases that are triggered by persistent angiogenesis.

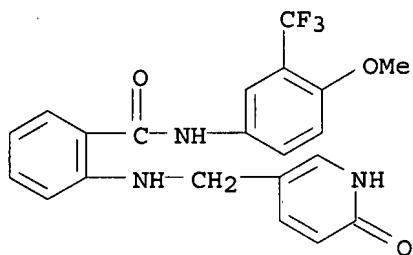
IT 811805-34-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyridonylmethyl anthranylamides as inhibitors of vascular endothelial growth factor receptors VEGFR-2 and VEGFR-3)

RN 811805-34-2 HCAPLUS

CN Benzamide, 2-[[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-methoxy-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2007 ACS.on STN

ACCESSION NUMBER: 2004:120827 HCAPLUS

DOCUMENT NUMBER: 140:181330

TITLE: Preparation of anthranylamidopyridines as inhibitors of vascular endothelial growth factor receptor-2 and -3 (VEGFR-2 and -3).

INVENTOR(S): Huth, Andreas; Krueger, Martin; Zorn, Ludwig; Ince, Stuart; Thierauch, Karl-Heinz; Menrad, Andreas;

Haberey, Martin; Hess-Stump, Holger Schering Aktiengesellschaft, Germany

PATENT ASSIGNEE(S): PCT Int: Appl., 88 pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

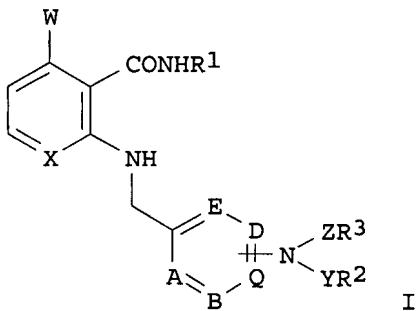
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013102	A1	20040212	WO 2003-EP7964	20030722
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10235690	A1	20040219	DE 2002-10235690	20020731
DE 10328036	A1	20050105	DE 2003-10328036	20030619

CA 2493026	A1	20040212	CA 2003-2493026	20030722
AU 2003281855	A1	20040223	AU 2003-281855	20030722
BR 2003013122	A	20050705	BR 2003-13122	20030722
CN 1671666	A	20050921	CN 2003-818334	20030722
EP 1594841	A1	20051116	EP 2003-740470	20030722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005538112	T	20051215	JP 2004-525272	20030722
NZ 537291	A	20070223	NZ 2003-537291	20030722
US 2004147535	A1	20040729	US 2003-631018	20030731
US 7148357	B2	20061212		
US 2005054654	A1	20050310	US 2004-870491	20040618
MX 2004PA12948	A	20050912	MX 2004-PA12948	20041217
IN 2005DN00309	A	20070119	IN 2005-DN309	20050127
NO 2005001035	A	20050429	NO 2005-1035	20050225
US 2007015794	A1	20070118	US 2006-525091	20060922
PRIORITY APPLN. INFO.:				
		DE 2002-10235690	A	20020731
		DE 2003-10328036	A	20030619
		US 2002-407970P	P	20020905
		US 2003-483896P	P	20030702
		WO 2003-EP7964	W	20030722
		US 2003-631018	A3	20030731

OTHER SOURCE(S) : MARPAT 140:181330

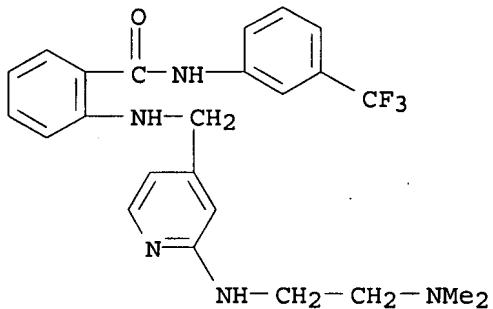
GI



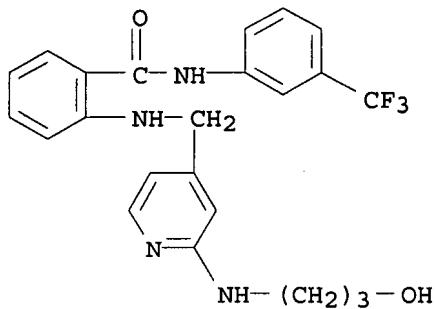
AB Title compds. [I; X = CH, N; W = H, F; A, B, D, E, Q = N, C; ≤ 2 of A, B, D, E, Q = N; R1 = (substituted) aryl, heteroaryl; Y, Z = bond, CO, CS, SO₂; R2, R3 = H, CONR9R10, SO₂R6, COR11, NR9R10, (substituted) alkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl; R2YNZAR3 = atoms to form a 3-8 membered (substituted) (unsatd.) ring; R6 = H, alkyl, haloalkyl, (substituted) aryl, heteroaryl, NR9R10; R9, R10 = H, alkyl, alkenyl, aryl, cycloalkyl, etc.; R11 = alkyl, alkoxy, hydroxyalkyl, hydroxyalkoxy, cycloalkyl, (substituted) Ph, pyridyl, biphenyl, naphthyl], were prepared Thus, 2-[(2-bromopyridin-4-ylmethyl)amino]-N-(3-trifluoromethylphenyl)benzamide (preparation given) pyridine, and N,N-dimethylaminoethylamine were heated in a pressure vessel for 5 h at 200° to give 2-[(2-dimethylaminoethylamino)pyridin-4-ylmethyl]amino]-N-(3-trifluoromethylphenyl)benzamide. I inhibited VEGFR-2 with IC₅₀ = 8-65 nM. I can be used for treatment of tumor or metastasis growth, psoriasis, Kaposi's sarcoma, restenosis, endometriosis, Crohn's disease, Hodgkin's disease, leukemia, arthritis, hemangioma, angiofibroma, eye disease, renal diseases, transplant rejection, fibrotic diseases, mesangial cell proliferative diseases, atherosclerosis, injuries to nervous tissue and for inhibition of the reocclusion of vessels after balloon catheter treatment, in vessel prosthetics, or after the application of mech. devices to hold open vessels, as immunosuppressants,

IT for scar-free wound healing, age spots and contact dermatitis.
 657399-79-6P, 2-[[2-(2-Dimethylaminoethylamino)pyridin-4-ylmethyl]amino]-N-(3-trifluoromethylphenyl)benzamide 657399-81-0P
 657399-82-1P 657399-83-2P 657399-84-3P
 657399-85-4P 657399-87-6P 657399-88-7P
 657399-93-4P 657399-97-8P 657399-98-9P
 657399-99-0P 657400-00-5P 657400-01-6P
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 657400-08-3P 657400-09-4P 657400-10-7P
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 657400-64-1P 657400-74-3P 657400-75-4P
 657400-95-8P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of anthranyl amidopyridines as inhibitors of vascular endothelial growth factor receptor)

RN 657399-79-6 HCAPLUS
 CN Benzamide, 2-[[2-[(dimethylamino)ethyl]amino]-4-pyridinylmethyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

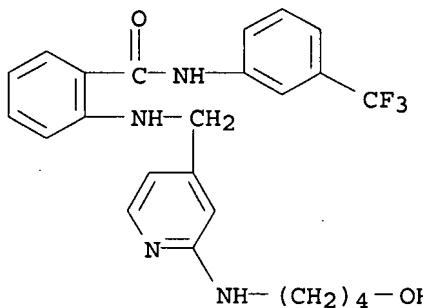


RN 657399-81-0 HCAPLUS
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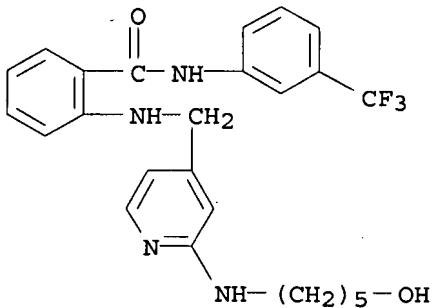
RN 657399-82-1 HCAPLUS
 CN Benzamide, 2-[[2-[(4-hydroxybutyl)amino]-4-pyridinylmethyl]amino]-N-[3-

(trifluoromethyl)phenyl] - (9CI) (CA INDEX NAME)



RN 657399-83-2 HCAPLUS

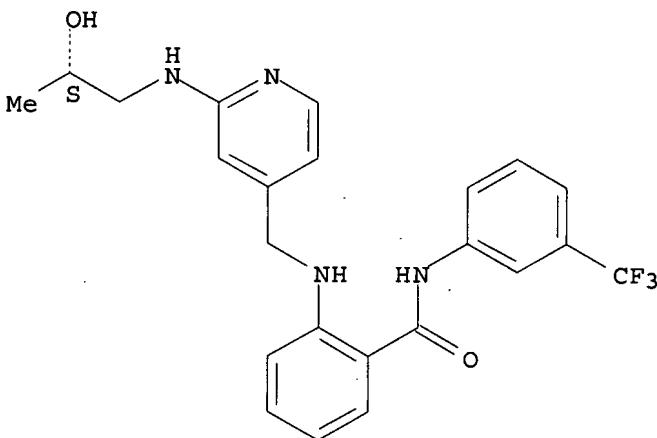
CN Benzamide, 2-[[2-[(5-hydroxypentyl)amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657399-84-3 HCAPLUS

CN Benzamide, 2-[[2-[[2-[(2S)-2-hydroxypropyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

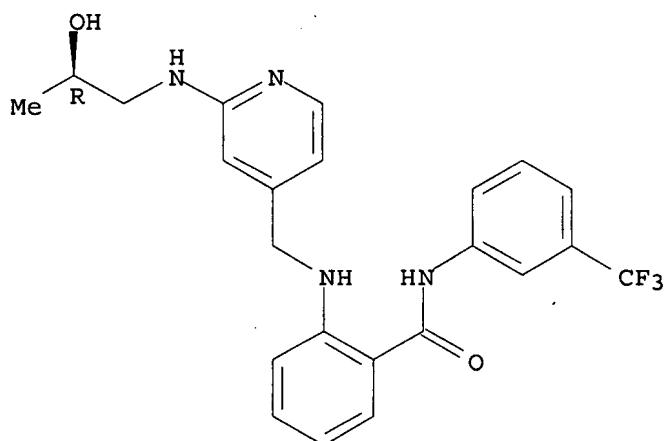


RN 657399-85-4 HCAPLUS

CN Benzamide, 2-[[2-[[2-[(2R)-2-hydroxypropyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Updated Search

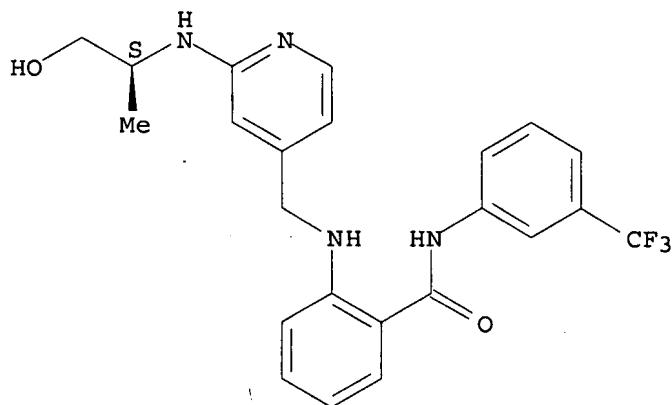
Absolute stereochemistry.



RN 657399-87-6 HCPLUS

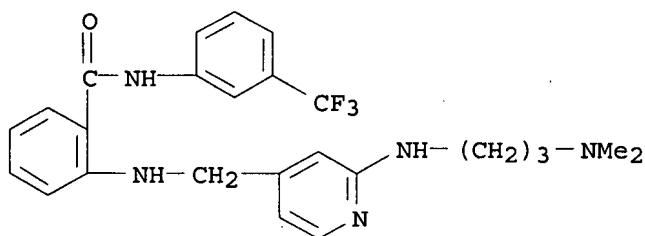
CN Benzamide, 2-[[2-[[1S]-2-hydroxy-1-methylethyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



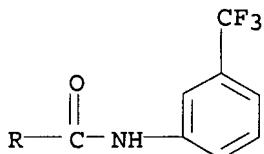
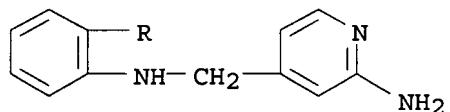
RN 657399-88-7 HCPLUS

CN Benzamide, 2-[[2-[[3-(dimethylamino)propyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

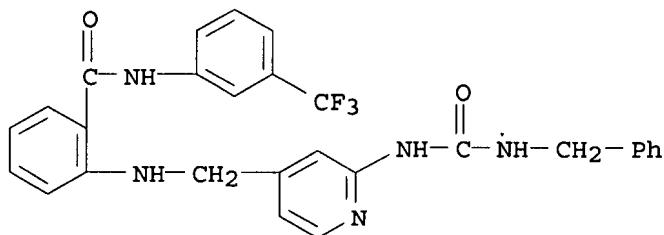


Updated Search

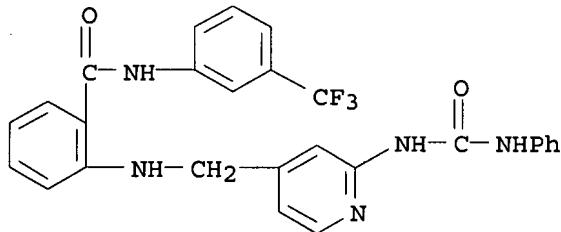
RN 657399-93-4 HCAPLUS
CN Benzamide, 2-[[[2-amino-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



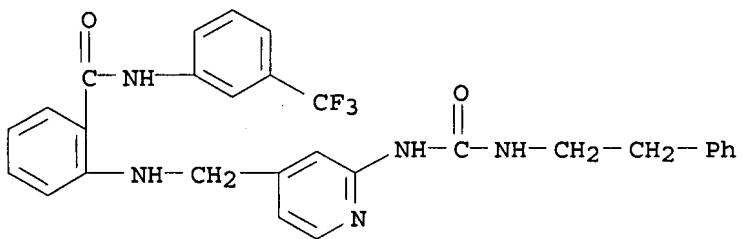
RN 657399-97-8 HCAPLUS
CN Benzamide, 2-[[[2-[[[(phenylmethyl)amino]carbonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



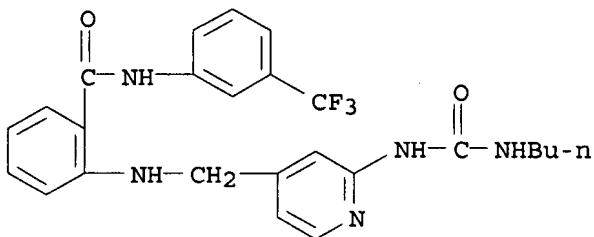
RN 657399-98-9 HCAPLUS
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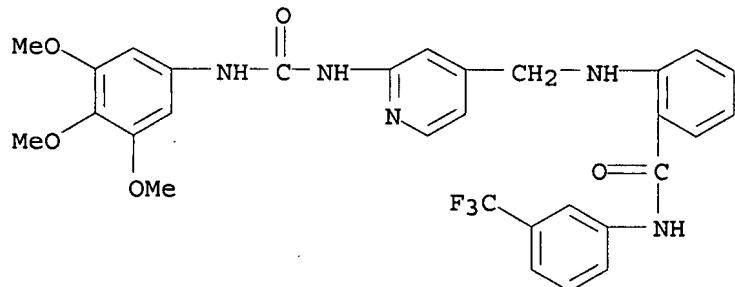
RN 657399-99-0 HCAPLUS
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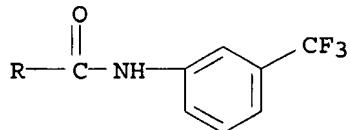
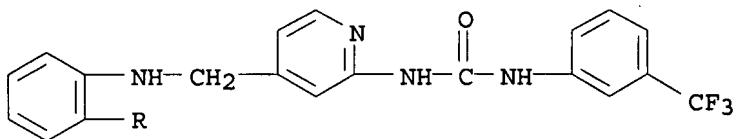
RN 657400-00-5 HCAPLUS
 CN Benzamide, 2-[[2-[[[butylamino]carbonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657400-01-6 HCAPLUS
 CN Benzamide, N-[3-(trifluoromethyl)phenyl]-2-[[[2-[[[3,4,5-trimethoxyphenyl]amino]carbonyl]amino]-4-pyridinyl]methyl]amino]- (9CI) (CA INDEX NAME)

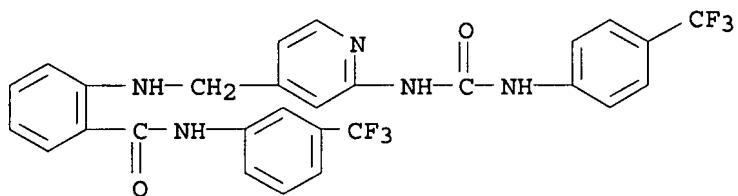


RN 657400-02-7 HCAPLUS
 CN Benzamide, N-[3-(trifluoromethyl)phenyl]-2-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-4-pyridinyl]methyl]amino]- (9CI) (CA INDEX NAME)



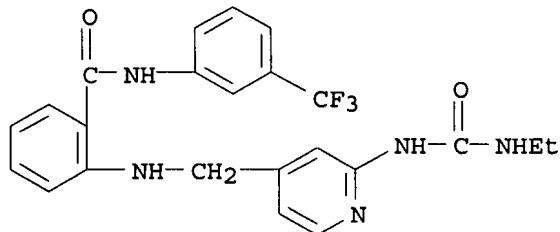
RN 657400-03-8 HCAPLUS

CN Benzamide, N-[3-(trifluoromethyl)phenyl]-2-[[2-[[[4-(trifluoromethyl)phenyl]amino]carbonyl]amino]-4-pyridinylmethyl]amino]-(9CI) (CA INDEX NAME)



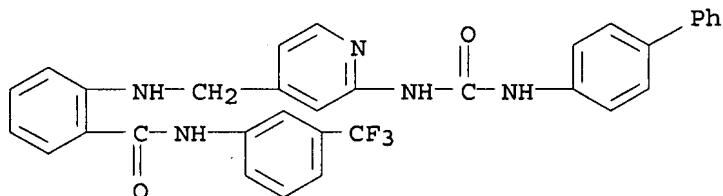
RN 657400-04-9 HCAPLUS

CN Benzamide, 2-[[2-[(ethylamino)carbonyl]amino]-4-pyridinylmethyl]amino]-N-[3-(trifluoromethyl)phenyl]-(9CI) (CA INDEX NAME)

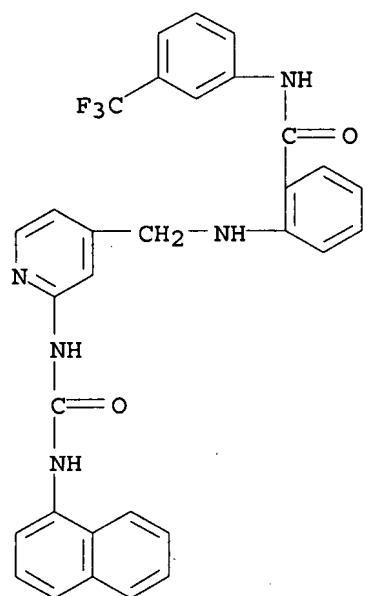


RN 657400-05-0 HCAPLUS

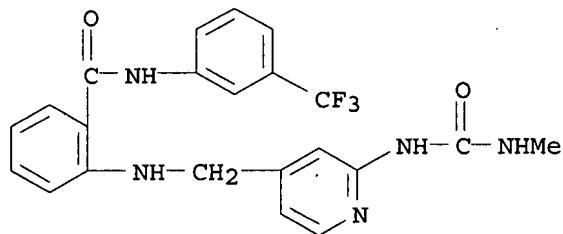
CN Benzamide, 2-[[2-[[[1,1'-biphenyl]-4-ylamino]carbonyl]amino]-4-pyridinylmethyl]amino]-N-[3-(trifluoromethyl)phenyl]-(9CI) (CA INDEX NAME)



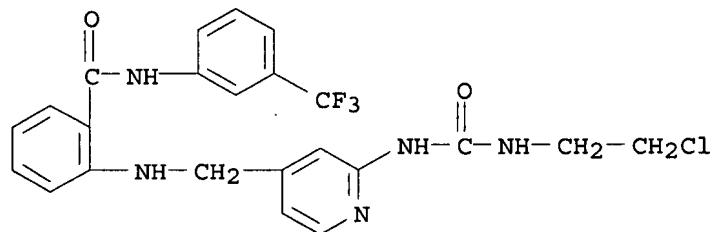
RN 657400-06-1 HCAPLUS
CN Benzamide, 2-[[2-[[[(1-naphthalenylamino)carbonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



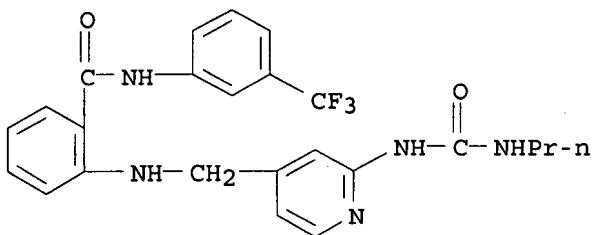
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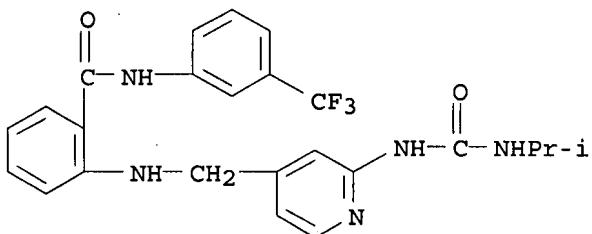
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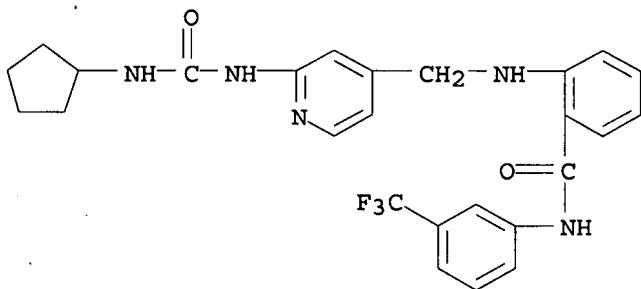
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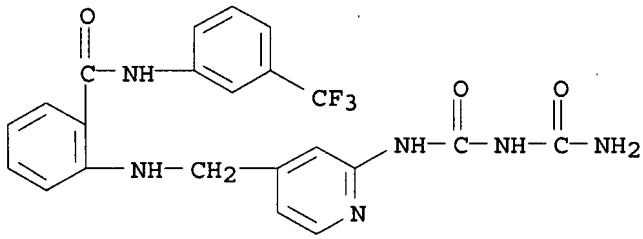
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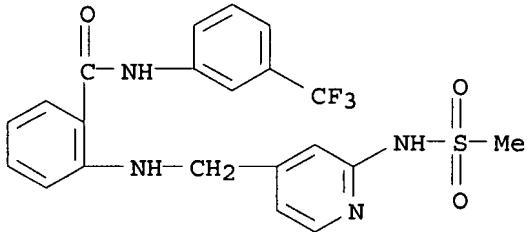
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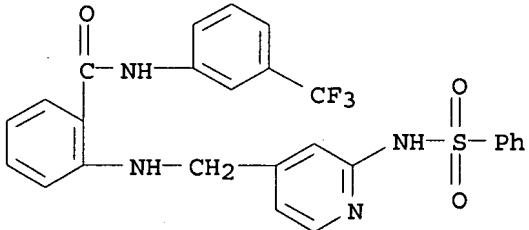
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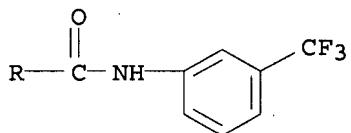
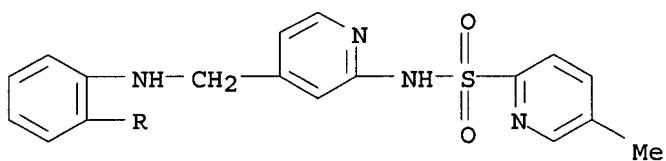
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RN 657400-38-9 HCAPLUS
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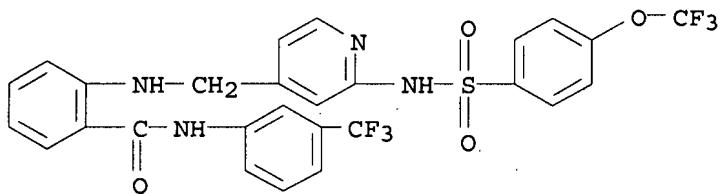


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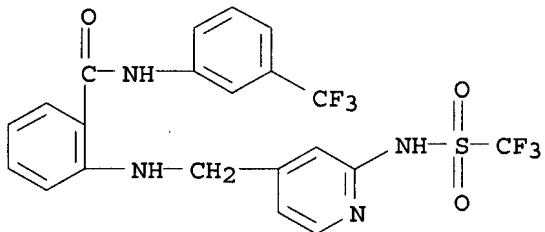
RN 657400-40-3 HCAPLUS

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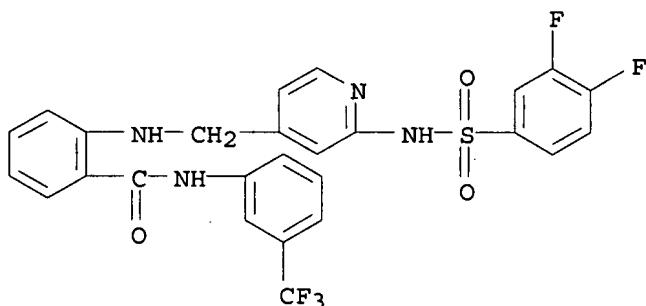
RN 657400-41-4 HCAPLUS

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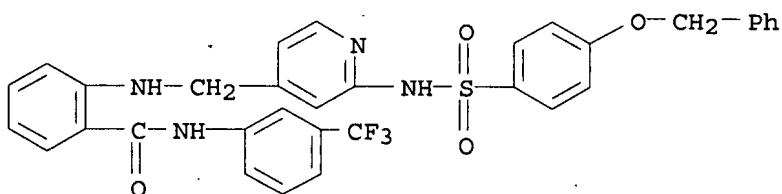
RN 657400-43-6 HCAPLUS

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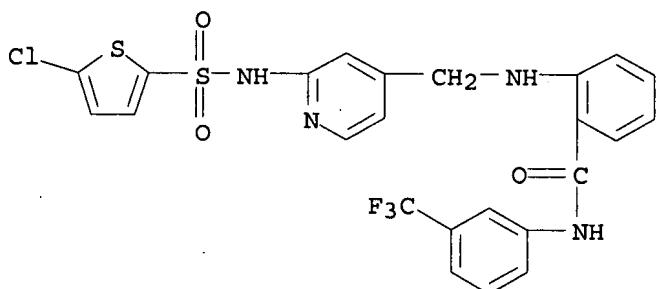
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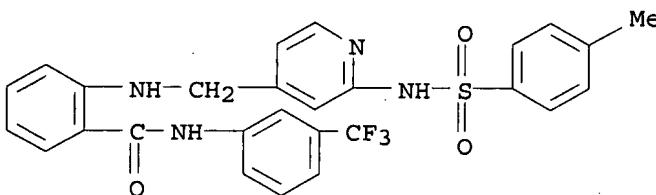
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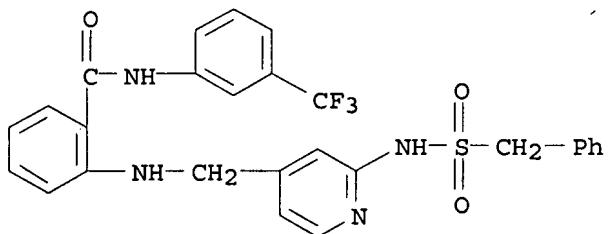


RN 657400-47-0 HCAPLUS

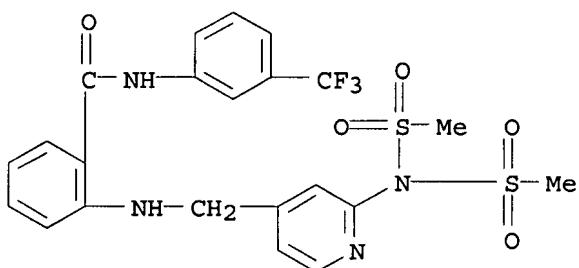
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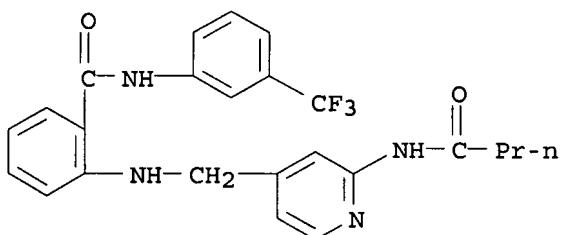
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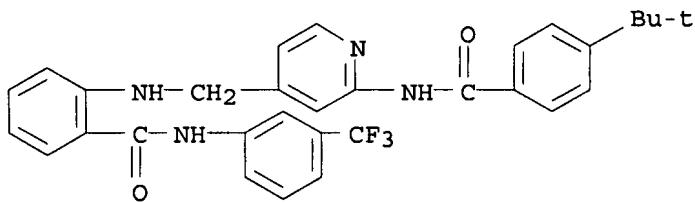
RN 657400-51-6 HCAPLUS
CN Benzamide, 2-[[2-[bis(methylsulfonyl)amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657400-53-8 HCAPLUS
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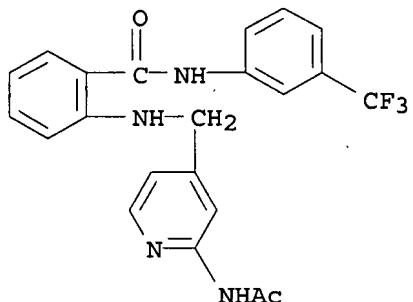


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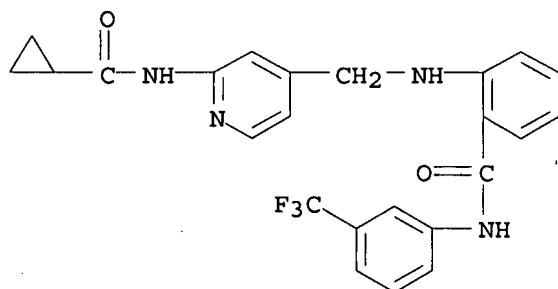
RN 657400-64-1 HCAPLUS

CN Benzamide, 2-[[2-(acetylamino)-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



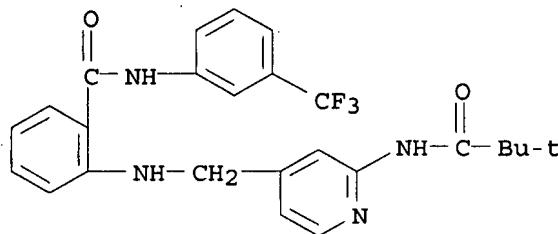
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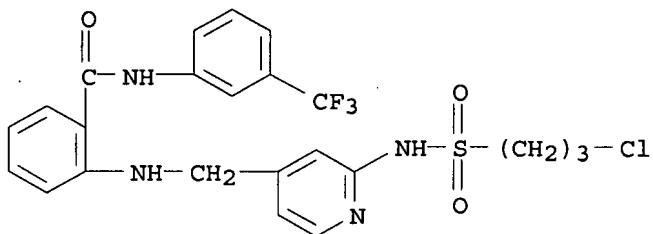


RN 657400-75-4 HCAPLUS

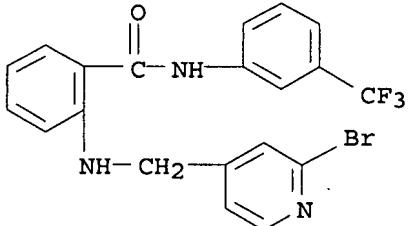
CN Benzamide, 2-[[2-[(2,2-dimethyl-1-oxopropyl)amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657400-95-8 HCAPLUS
CN Benzamide, 2-[[[2-[[[3-chloropropyl]sulfonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



IT 657401-06-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of anthranyl amidopyridines as inhibitors of vascular endothelial growth factor receptor)
RN 657401-06-4 HCAPLUS
CN Benzamide, 2-[[2-bromo-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:950057 HCAPLUS
DOCUMENT NUMBER: 140:16647
TITLE: Preparation of 2-aminopyridine-3-carboxamides as remedies for angiogenesis mediated diseases
INVENTOR(S): Askew, Benny; Adams, Jeffrey; Booker, Shon; Chen, Guoqing; DiPietro, Lucian V.; Elbaum, Daniel; Germain, Julie; Geuns-Meyer, Stephanie D.; Habgood, Gregory J.; Handley, Michael; Huang, Qi; Kim, Tae-seong; Li, Aiwen; Nishimura, Nobuko; Nomak, Rana; Patel, Vinod F.; Riahi, Babak; Kim, Joseph L.; Xi, Ning; Yang, Kevin; Yuan, Chester Chenguang
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 252 pp., Cont.-in-part of U.S. Ser. No. 46,681.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

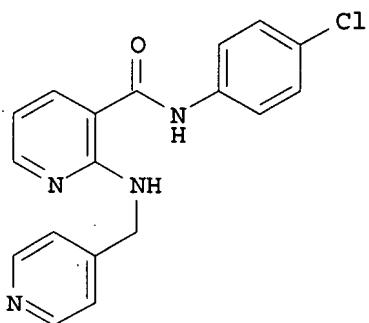
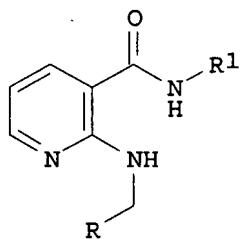
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2003225106	A1	20031204	US 2002-197974	20020717
US 6878714	B2	20050412		
US 2003125339	A1	20030703	US 2002-46681	20020110
US 6995162	B2	20060207		
AT 361288	T	20070515	AT 2002-717325	20020111
EP 1798230	A1	20070620	EP 2007-3413	20020111
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CA 2492100	A1	20040122	CA 2003-2492100	20030715
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BG 108012	A	20041130	BG 2003-108012	20030721
US 2005261313	A1	20051124	US 2004-14184	20041215
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US 2001-261339P P 20010112				
US 2001-323764P P 20010919				
US 2002-46681 A2 20020110				
AU 2002-248340 A3 20020111				
EP 2002-717325 A3 20020111				
US 2002-197974 A 20020717				
WO 2003-US22417 W 20030715				

OTHER SOURCE(S):

GI

MARPAT 140:16647



AB The title compds. [I; R = (un)substituted 4-pyridyl, 2-pyridyl, 4-pyrimidinyl, 4-quinolyl, etc.; R1 = (un)substituted aryl, cycloalkyl, 5-6 membered heteroaryl, 9-10 membered bicyclic and 11-14 membered tricyclic heterocycl], which are effective for prophylaxis and treatment

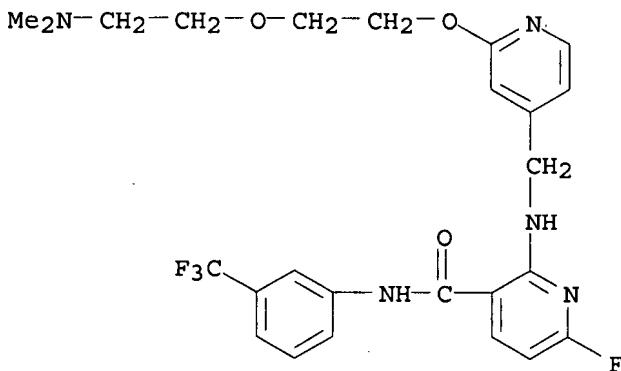
of diseases and other maladies or conditions involving, cancer and the like, were prepared. Thus, the title compound II was prepared from 2-aminonicotinic acid, 4-chloroaniline, and 4-pyridinecarboxaldehyde. The compds. I showed inhibition of KDR kinase at < 50 μ M. Many compds. I inhibited VEGF-stimulated HUVEC proliferation at a level below 50 nM. Pharmaceutical composition comprising the compound I is claimed.

IT 453563-07-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-aminopyridine-3-carboxamides for treating angiogenesis mediated diseases)

RN 453563-07-0 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[2-[2-[2-(dimethylamino)ethoxy]ethoxy]-4-pyridinyl]methyl]amino]-6-fluoro-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

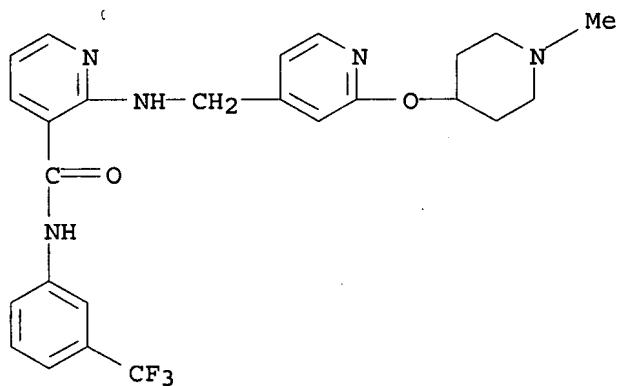


IT 453561-97-2P 453563-29-6P 453563-38-7P
453563-56-9P 453563-57-0P 453563-72-9P
453563-75-2P 453563-83-2P 453563-98-9P
453564-12-0P 453564-27-7P 453564-30-2P
453564-80-2P 629650-87-9P 629650-88-0P
629650-89-1P 629650-90-4P 629650-93-7P
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629651-53-2P 629651-58-7P 629651-99-6P
629652-02-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aminopyridine-3-carboxamides for treating angiogenesis mediated diseases)

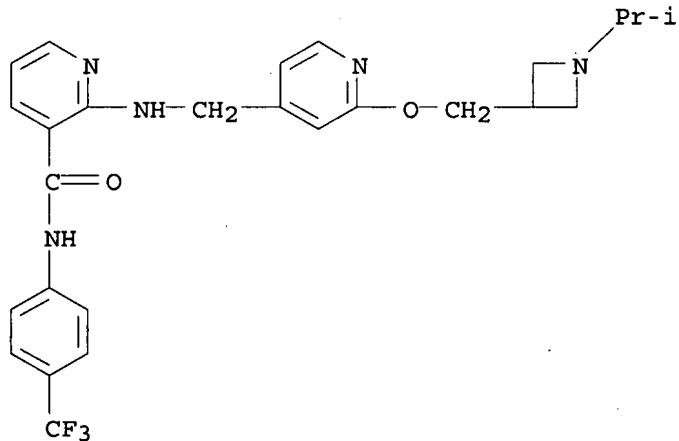
RN 453561-97-2 HCAPLUS

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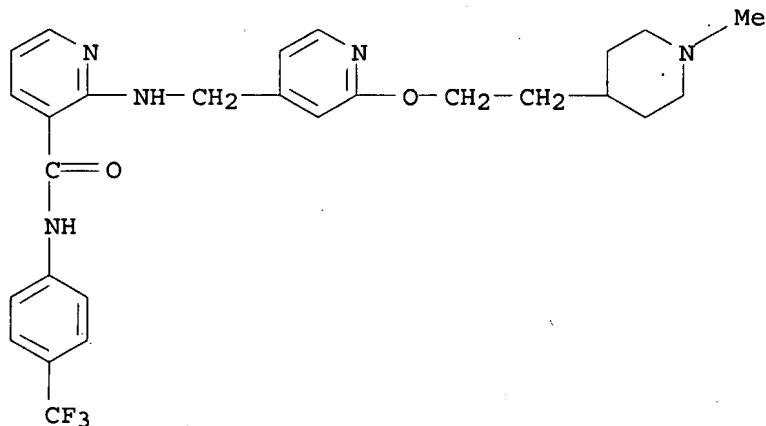
RN 453563-29-6 HCAPLUS

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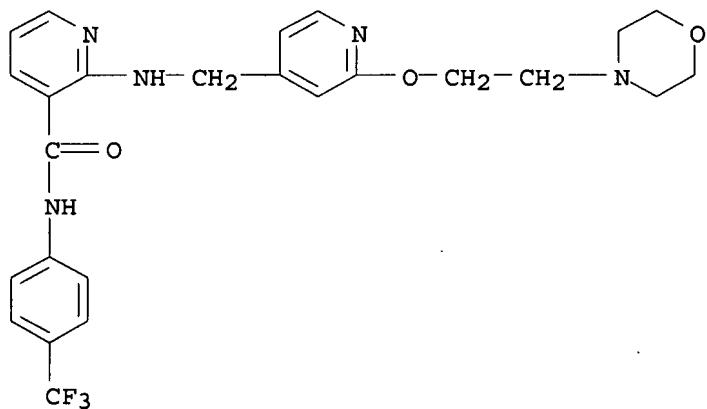


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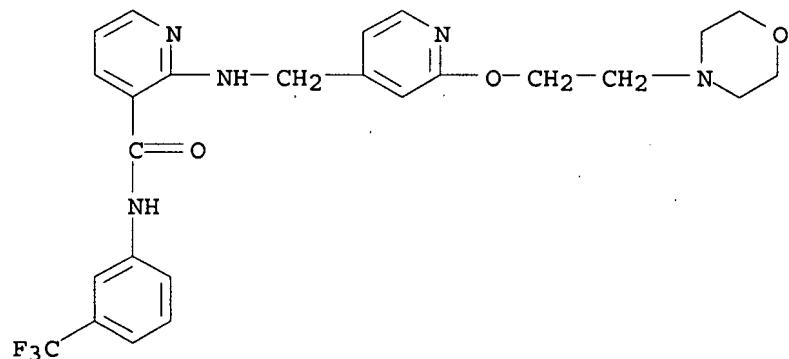
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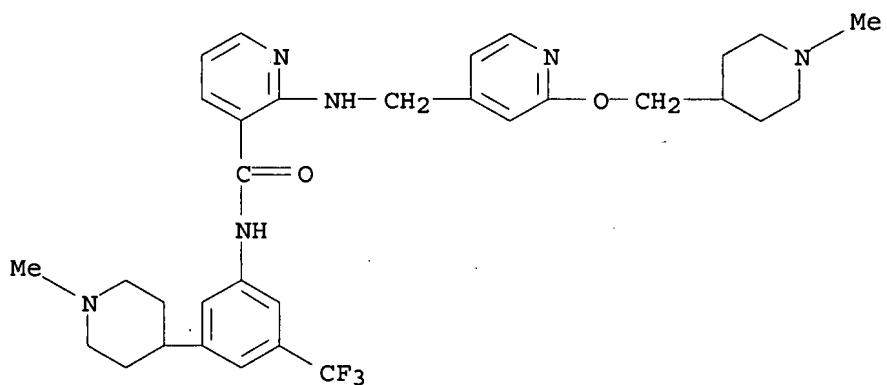
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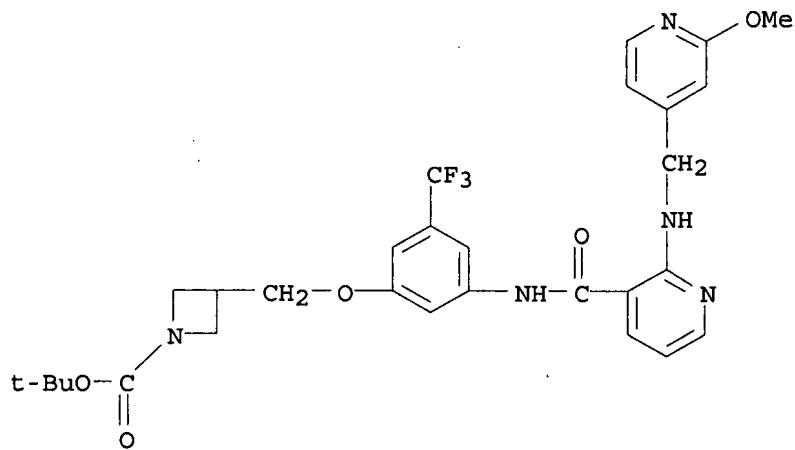
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CN 3-Pyridinecarboxamide, 2-[[2-[2-(4-morpholinyl)ethoxy]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



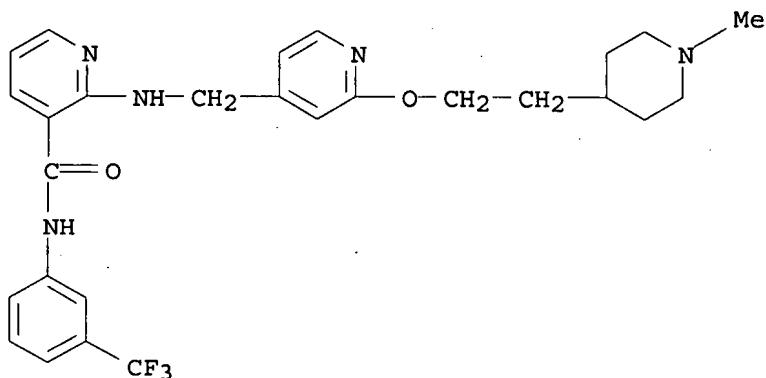
RN 453563-72-9 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[2-[(1-methyl-4-piperidinyl)methoxy]-4-pyridinyl]methyl]amino]-N-[3-(1-methyl-4-piperidinyl)-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



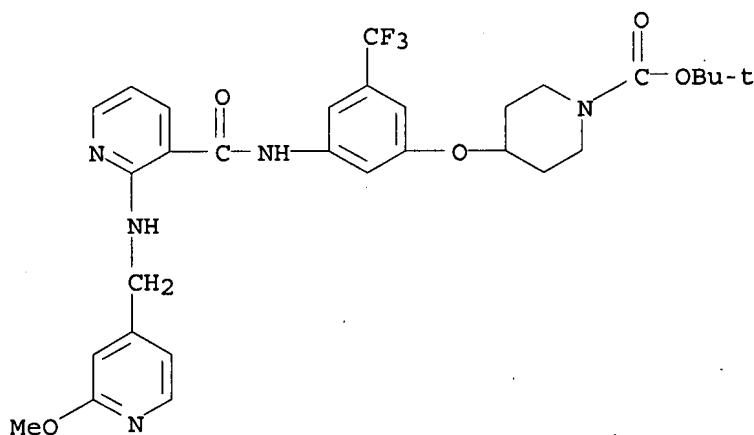
RN 453563-75-2 HCAPLUS
 CN 1-Azetidinecarboxylic acid, 3-[[3-[[2-[[2-methoxy-4-pyridinyl]methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenoxy]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



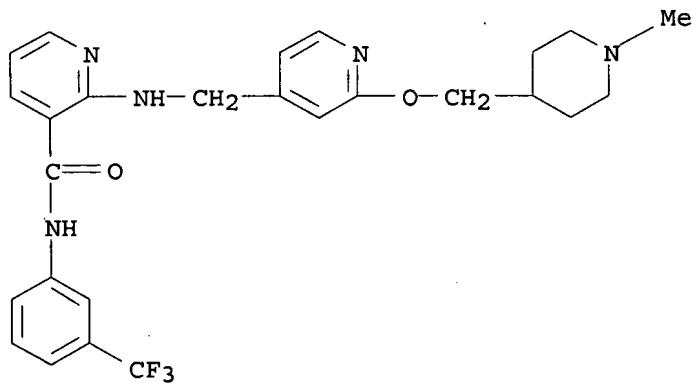
RN 453563-83-2 HCAPLUS
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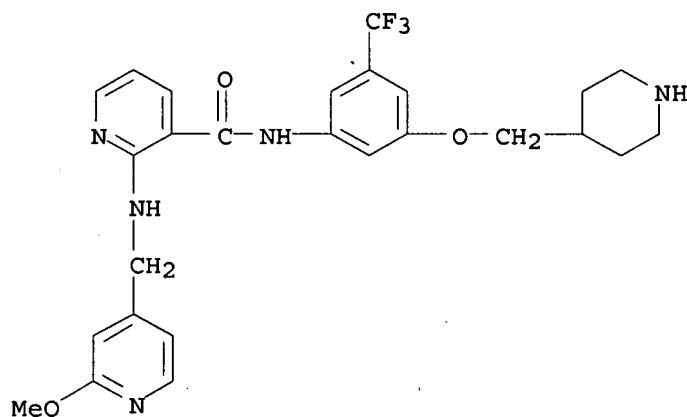
RN 453563-98-9 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[3-[[2-[(2-methoxy-4-pyridinyl)methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 453564-12-0 HCAPLUS
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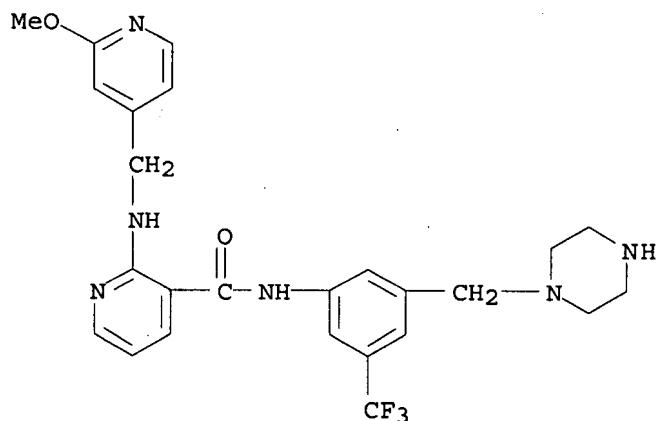


RN 453564-27-7 HCAPLUS
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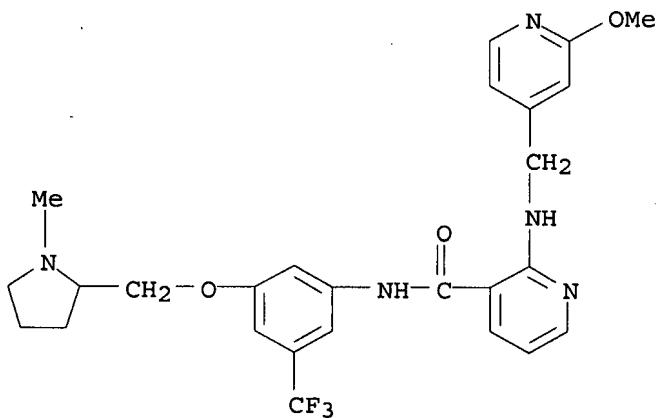
RN 453564-30-2 HCAPLUS

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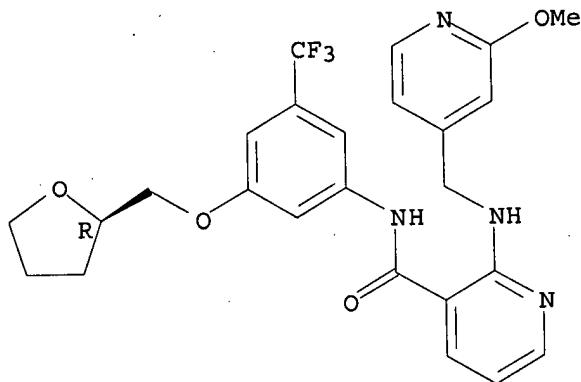
RN 453564-80-2 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[(1-methyl-2-pyrrolidinyl)methoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



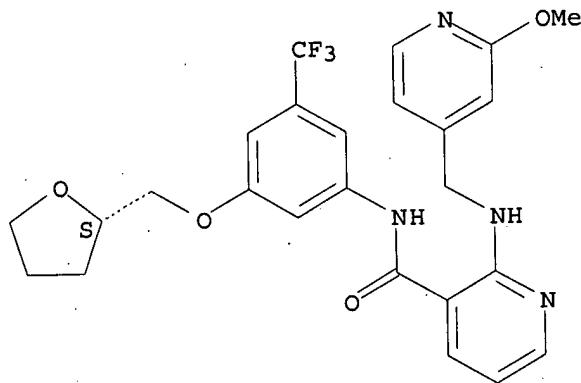
RN 629650-87-9 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-
[(2R)-tetrahydro-2-furanyl]methoxy]-5-(trifluoromethyl)phenyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



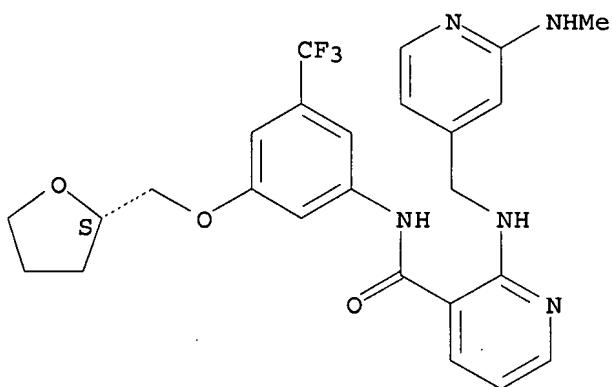
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CN 3-Pyridinecarboxamide, 2-[[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-
[(2S)-tetrahydro-2-furanyl]methoxy]-5-(trifluoromethyl)phenyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 629650-89-1 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl)methyl]amino]-N-[3-
[(2S)-tetrahydro-2-furanyl]methoxy]-5-(trifluoromethyl)phenyl]- (9CI)
(CA INDEX NAME)

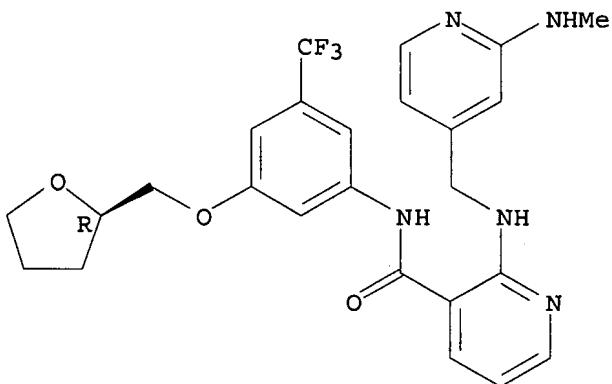
Absolute stereochemistry.



RN 629650-90-4 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl]methyl]amino]-N- [3-[(2R)-tetrahydro-2-furanyl]methoxy]-5-(trifluoromethyl)phenyl]- (9CI)
(CA INDEX NAME)

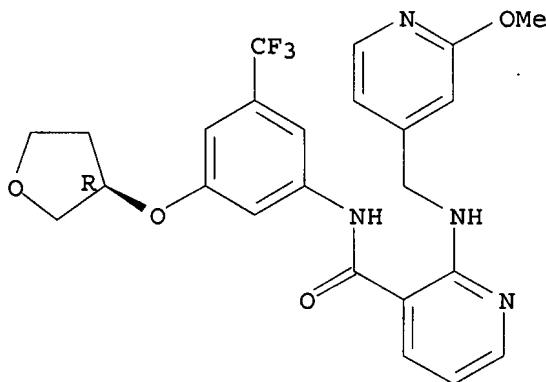
Absolute stereochemistry.



RN 629650-93-7 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-methoxy-4-pyridinyl)methyl]amino]-N- [3-[(3R)-tetrahydro-3-furanyl]oxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

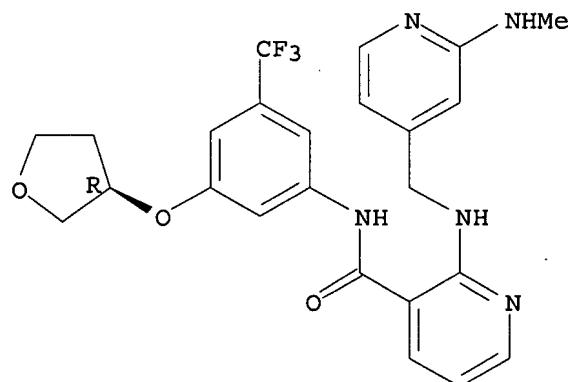
Absolute stereochemistry.



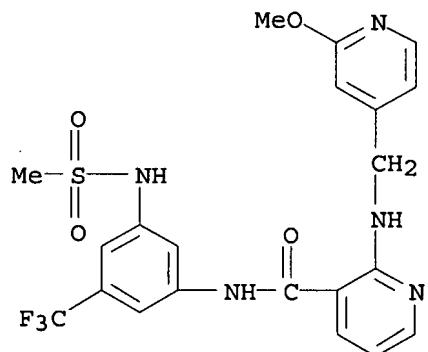
Updated Search

RN 629650-94-8 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl]methyl]amino]-N-[3-[(3R)-tetrahydro-3-furanyl]oxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

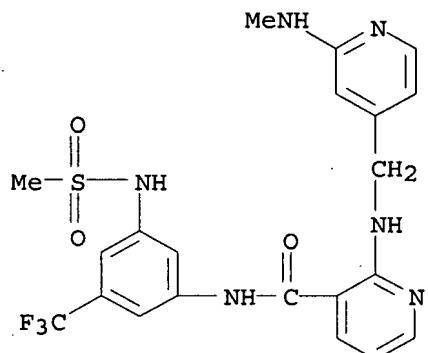
Absolute stereochemistry.



RN 629651-03-2 HCAPLUS
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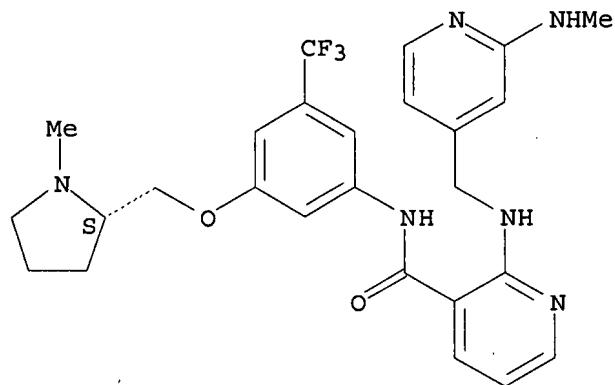


RN 629651-05-4 HCAPLUS
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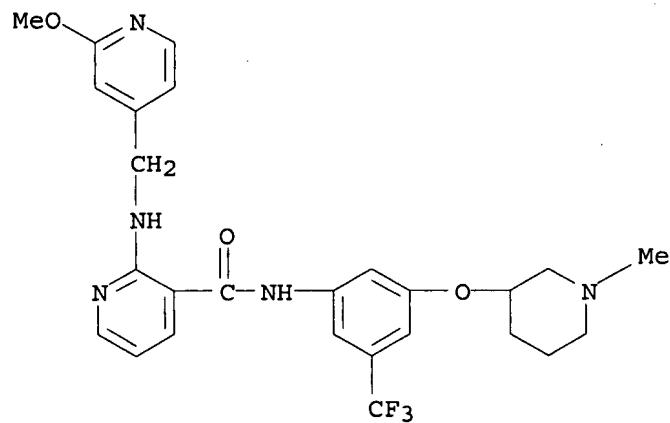


RN 629651-53-2 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl]methyl]amino]-N-[3-[(2S)-1-methyl-2-pyrrolidinyl]methoxy]-5-(trifluoromethyl)phenyl]- (9CI)
(CA INDEX NAME)

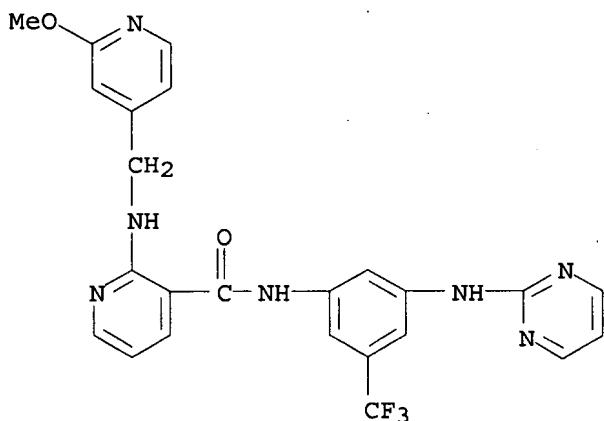
Absolute stereochemistry.



RN 629651-58-7 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[(1-methyl-3-piperidinyl)oxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

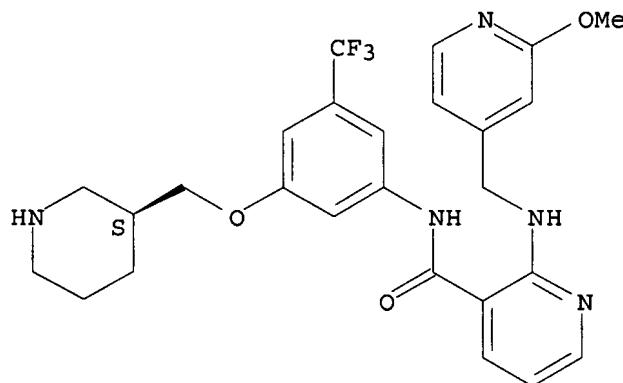


RN 629651-99-6 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-methoxy-4-pyridinyl)methyl]amino]-N-[3-(2-pyrimidinylamino)-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 629652-02-4 HCAPLUS
 CN 3-Pyridinecarboxamide, 2-[[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[(3S)-3-piperidinylmethoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2002:868928 HCAPLUS
 DOCUMENT NUMBER: 137:352900
 TITLE: Selective anthranilamide pyridine amides as inhibitors of VEGFR-2 and VEGFR-3
 INVENTOR(S): Ernst, Alexander; Huth, Andreas; Krueger, Martin; Thierauch, Karl-Heinz; Menrad, Andreas; Haberey, Martin
 PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
 SOURCE: PCT Int. Appl., 115 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002090352	A2	20021114	WO 2002-EP4924	20020503

WO 2002090352

A3 20030501

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW

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GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10123574	A1	20021128	DE 2001-10123574	20010508
DE 10125294	A1	20021121	DE 2001-10125294	20010515
DE 10164590	A1	20030710	DE 2001-10164590	20011221
CA 2453223	A1	20021114	CA 2002-2453223	20020503
AU 2002310800	A1	20021118	AU 2002-310800	20020503
EP 1392680	A2	20040303	EP 2002-735333	20020503

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BR 2002009485	A	20040706	BR 2002-9485	20020503
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JP 2004528379	T	20040916	JP 2002-587431	20020503
RU 2299208	C2	20070520	RU 2003-134148	20020503
MX 2003PA10099	A	20040310	MX 2003-PA10099	20031105
IN 2003DN02076	A	20060120	IN 2003-DN2076	20031203
ZA 2003009434	A	20050905	ZA 2003-9434	20031204
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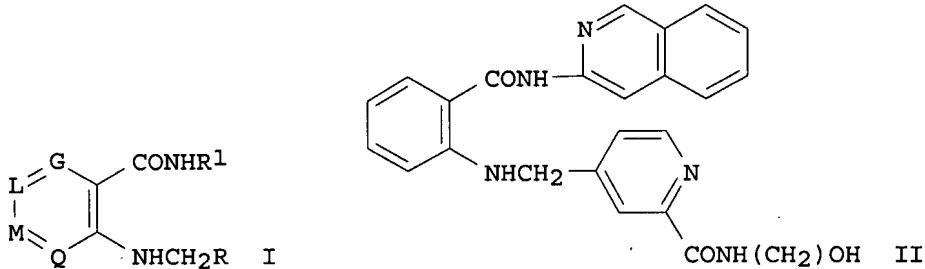
PRIORITY APPLN. INFO.:

DE	2001-10123574	A	20010508
DE	2001-10125294	A	20010515
DE	2001-10164590	A	20011221
WO	2002-EP4924	W	20020503

OTHER SOURCE(S) :

MARPAT 137:352900

GI



AB Title compds. I [G, L, M, Q = N, (un)substituted CH, \leq 1 of them being N; R = (un)substituted N heterocycle; R1 = (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl] were prepared I are inhibitors of VEGFR-2 and VEGFR-3 and are used as medicaments for treating diseases that are caused by persistent angiogenesis, such as psoriasis, Kaposi's sarcoma, restenosis, such as e.g. stent-induced restenosis, endometriosis, Crohn's disease, Hodgkin's disease, leukemia, arthritis, such as rheumatoid arthritis, hemangioma, angiofibromatosis, in eye diseases such as diabetic retinopathy, neovascular glaucoma, in kidney diseases such as glomerulonephritis, diabetic nephropathy, malign nephrosclerosis, thrombic micro-angiopathic syndrome, transplant rejection and glomerulopathy, in fibrotic diseases such as hepatic cirrhosis, mesangial-cell proliferative diseases, arteriosclerosis, damage to the

nerve tissue and inhibition of the re-occlusion of vessels after balloon catheter treatment, in vessel prosthetics or after the use of mech. devices for keeping vessels open, e.g. stents, as immunosuppressants, to support wound healing without scars and in cases of age spots and contact dermatitis. I can also be used as inhibitors of VEGFR-3 in lymphangiogenesis for hyperplastic and dysplastic changes in the lymphatic system. Thus, 2-amino-N-isoquinolin-3-ylbenzamide was treated with 2-bromo-5-pyridinecarboxaldehyde, followed by carboxylation and amidation to give the amide II. II had IC₅₀ for inhibition of VEGFR-2 of 40 nM and for inhibition of cytochrome 450 isoenzyme 2C9 of 2.9 μM.

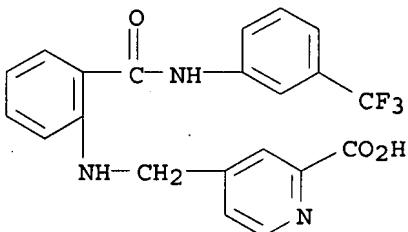
IT 474799-40-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of isoquinolinylcarbamoylphenylaminomethylpyridinecarboxamides as VEGFR-2 and VEGFR-3 inhibitors)

RN 474799-40-1 HCPLUS

CN 2-Pyridinecarboxylic acid, 4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbo- nyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



IT 474798-53-3P 474798-54-4P 474798-55-5P

474798-56-6P 474798-57-7P 474798-58-8P

474798-59-9P 474798-60-2P 474798-61-3P

474798-62-4P 474798-63-5P 474798-64-6P

474798-65-7P 474798-66-8P 474798-67-9P

474798-68-0P 474798-75-9P 474798-76-0P

474798-77-1P 474798-78-2P 474798-79-3P

474798-80-6P 474798-81-7P 474798-82-8P

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474798-86-2P 474798-87-3P 474798-88-4P

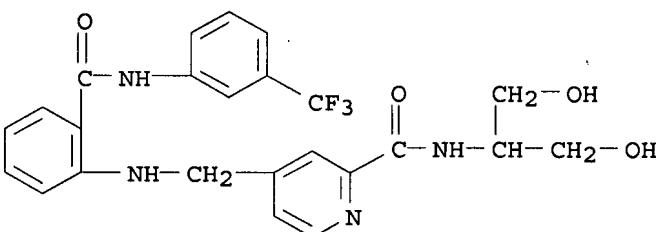
474798-89-5P 474798-90-8P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

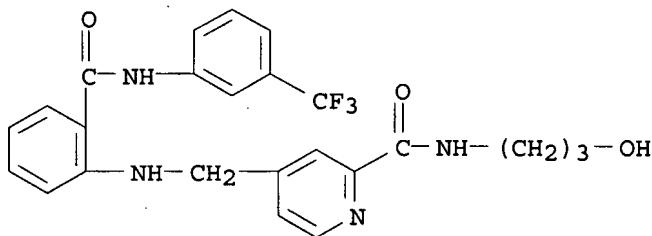
(preparation of isoquinolinylcarbamoylphenylaminomethylpyridinecarboxamides as VEGFR-2 and VEGFR-3 inhibitors)

RN 474798-53-3 HCPLUS

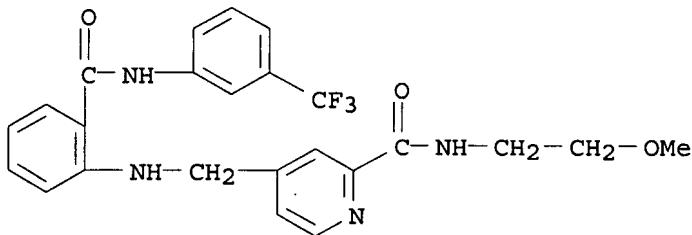
CN 2-Pyridinecarboxamide, N-[2-hydroxy-1-(hydroxymethyl)ethyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



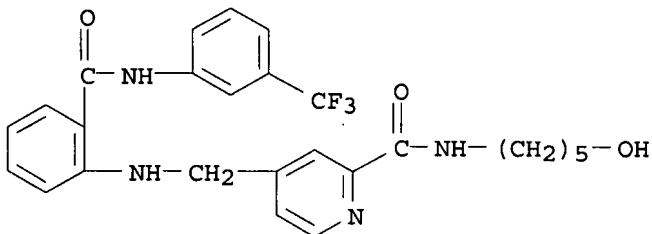
RN 474798-54-4 HCAPLUS
CN 2-Pyridinecarboxamide, N-(3-hydroxypropyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



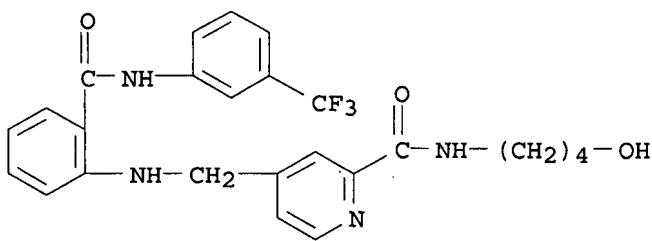
RN 474798-55-5 HCAPLUS
CN 2-Pyridinecarboxamide, N-(2-methoxyethyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 474798-56-6 HCAPLUS
CN 2-Pyridinecarboxamide, N-(5-hydroxypentyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



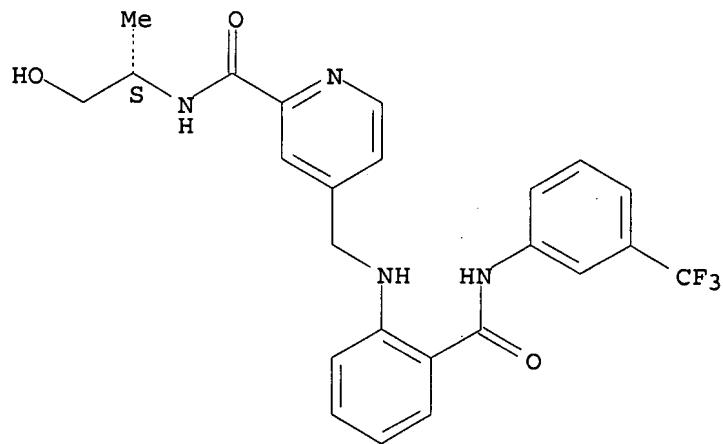
RN 474798-57-7 HCAPLUS
CN 2-Pyridinecarboxamide, N-(4-hydroxybutyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 474798-58-8 HCPLUS

CN 2-Pyridinecarboxamide, N-[(1S)-2-hydroxy-1-methylethyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

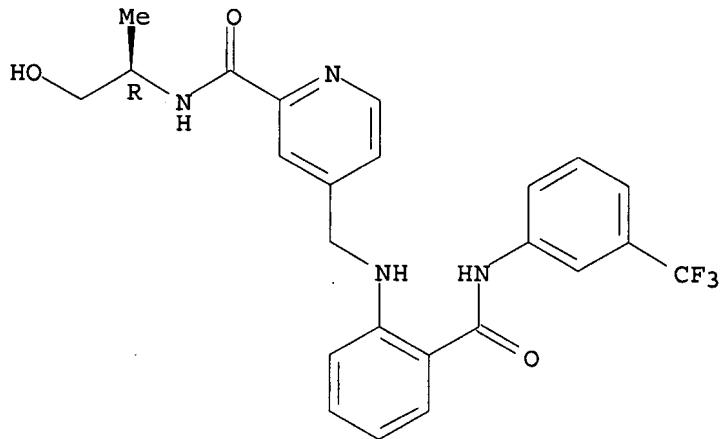
Absolute stereochemistry.



RN 474798-59-9 HCPLUS

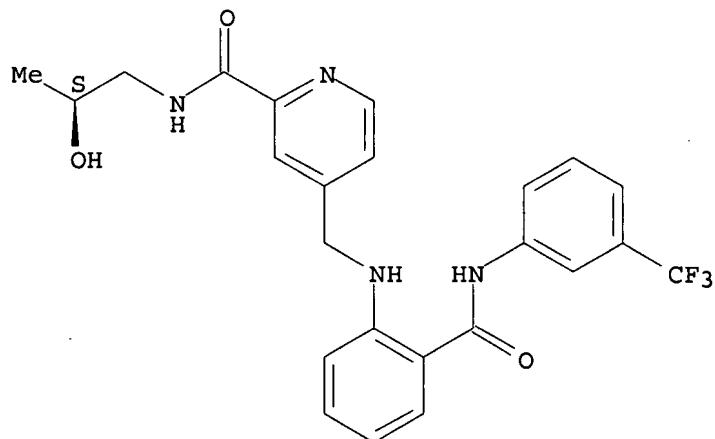
CN 2-Pyridinecarboxamide, N-[(1R)-2-hydroxy-1-methylethyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



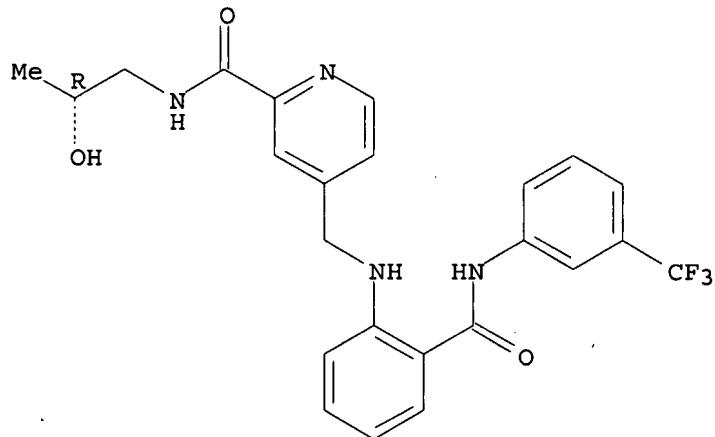
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Absolute stereochemistry.

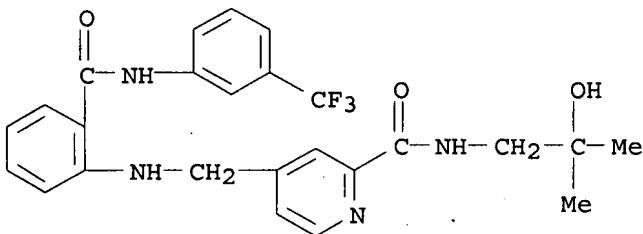


RN 474798-61-3 HCAPLUS
CN 2-Pyridinecarboxamide, N-[(2R)-2-hydroxypropyl]-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

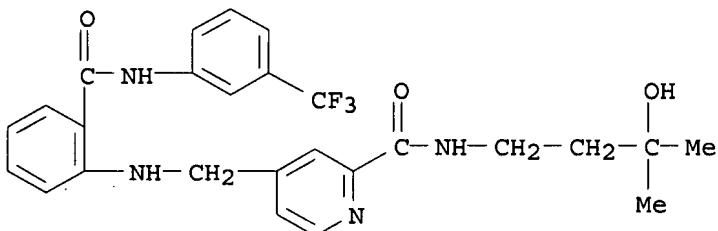


RN 474798-62-4 HCAPLUS
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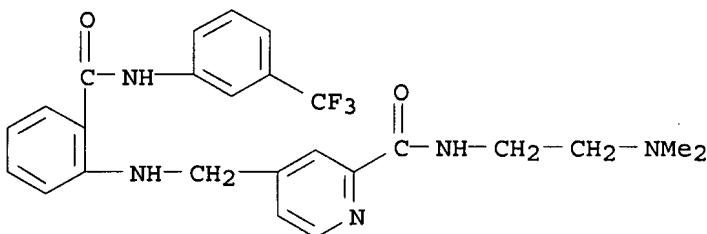
RN 474798-63-5 HCAPLUS

CN 2-Pyridinecarboxamide, N- (3-hydroxy-3-methylbutyl)-4- [[[2- [[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



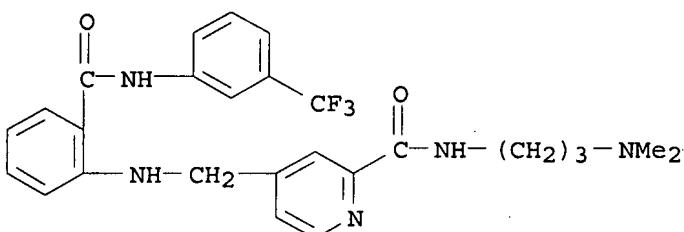
RN 474798-64-6 HCAPLUS

CN 2-Pyridinecarboxamide, N- [2- (dimethylamino)ethyl]-4- [[[2- [[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

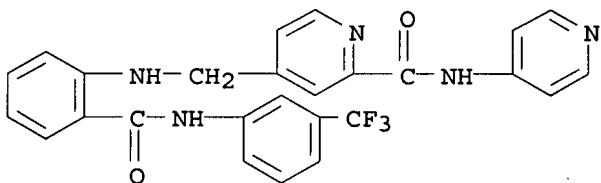


RN 474798-65-7 HCAPLUS

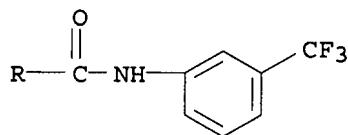
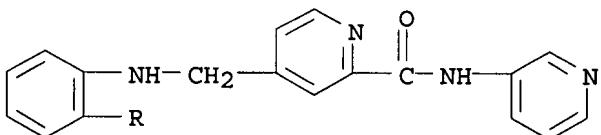
CN 2-Pyridinecarboxamide, N- [3- (dimethylamino)propyl]-4- [[[2- [[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



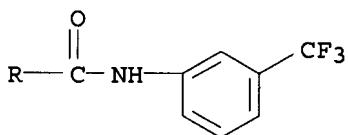
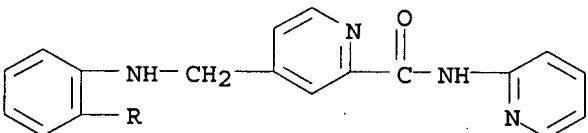
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CN 2-Pyridinecarboxamide, N-4-pyridinyl-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



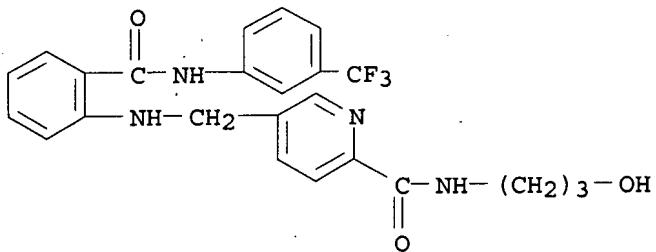
RN 474798-67-9 HCAPLUS
CN 2-Pyridinecarboxamide, N-3-pyridinyl-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 474798-68-0 HCAPLUS
CN 2-Pyridinecarboxamide, N-2-pyridinyl-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



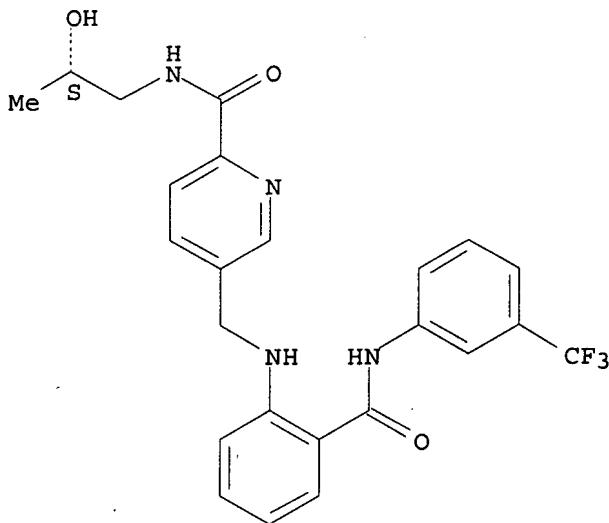
RN 474798-75-9 HCAPLUS
CN 2-Pyridinecarboxamide, N-(3-hydroxypropyl)-5-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 474798-76-0 HCPLUS

CN 2-Pyridinecarboxamide, N-[(2S)-2-hydroxypropyl]-5-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

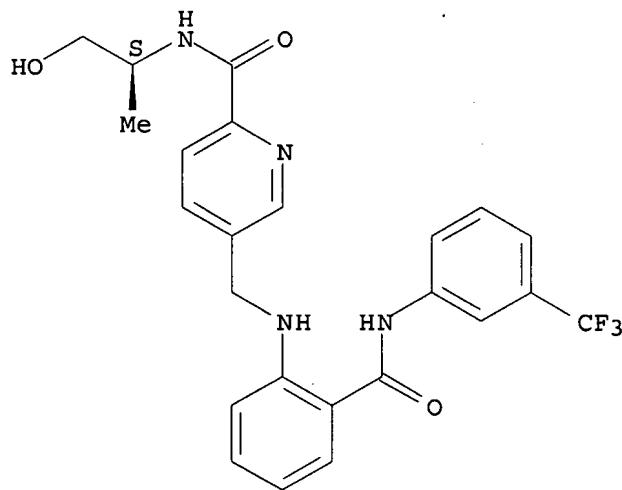
Absolute stereochemistry.



RN 474798-77-1 HCPLUS

CN 2-Pyridinecarboxamide, N-[(1S)-2-hydroxy-1-methylethyl]-5-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

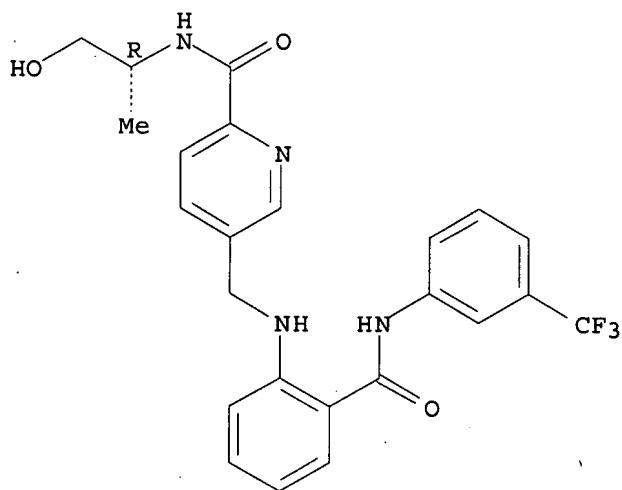
Absolute stereochemistry.



RN 474798-78-2 HCPLUS

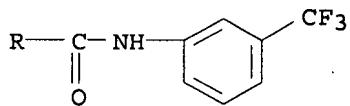
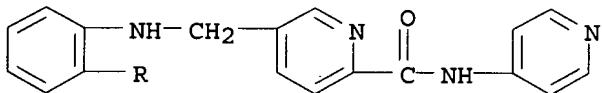
CN 2-Pyridinecarboxamide, N-[(1R)-2-hydroxy-1-methylethyl]-5-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



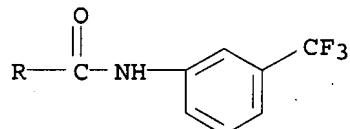
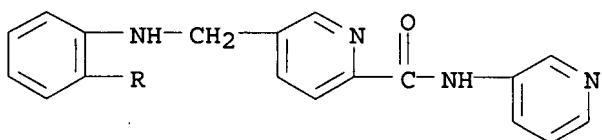
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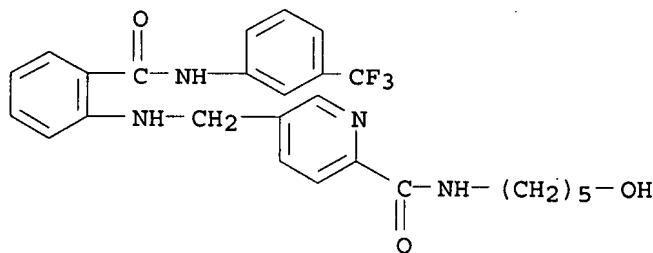


Updated Search

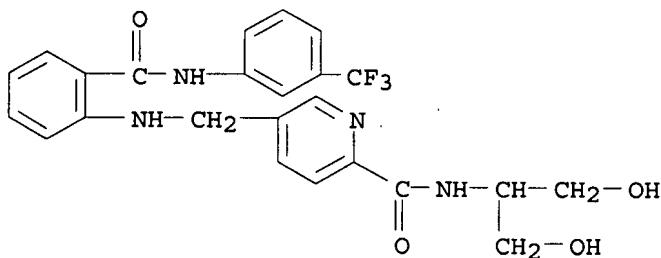
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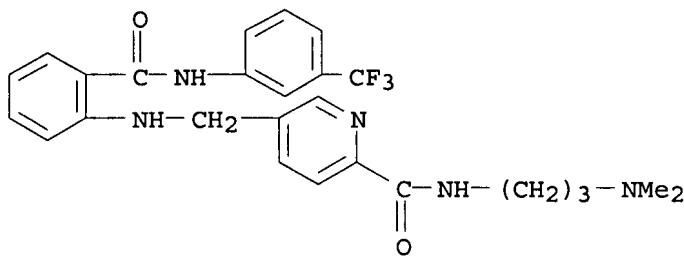
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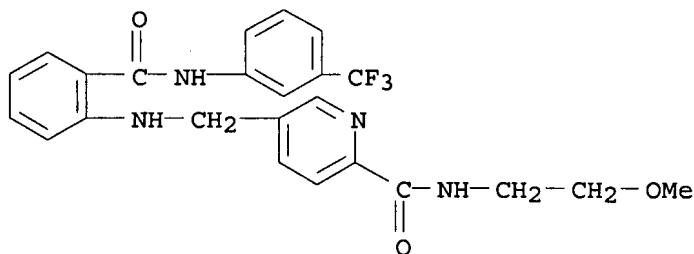
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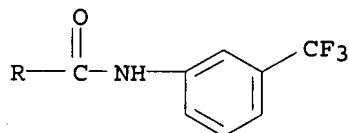
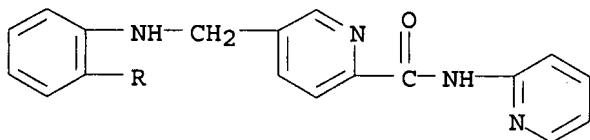
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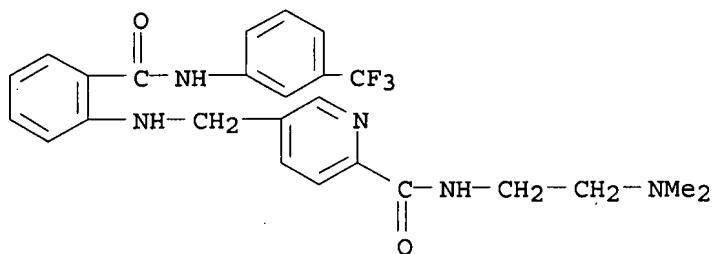
RN 474798-84-0 HCAPLUS
 CN 2-Pyridinecarboxamide, N-(2-methoxyethyl)-5-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 474798-85-1 HCAPLUS
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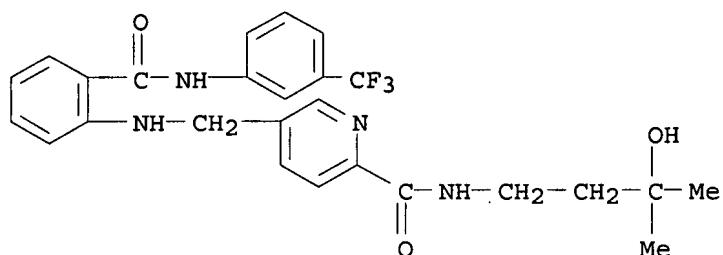


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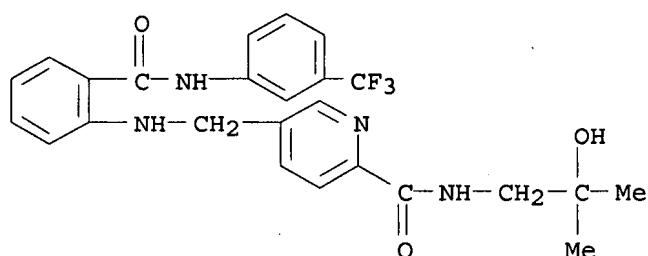
RN 474798-87-3 HCAPLUS

CN 2-Pyridinecarboxamide, N-(3-hydroxy-3-methylbutyl)-5-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl- (9CI) (CA INDEX NAME)



RN 474798-88-4 HCAPLUS

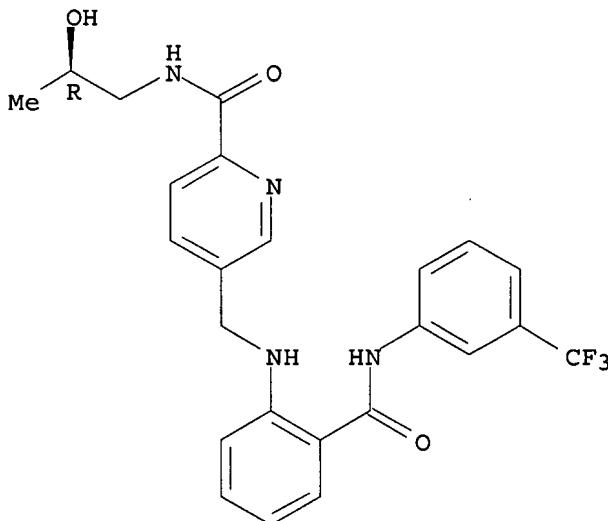
CN 2-Pyridinecarboxamide, N-(2-hydroxy-2-methylpropyl)-5-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl- (9CI) (CA INDEX NAME)



RN 474798-89-5 HCAPLUS

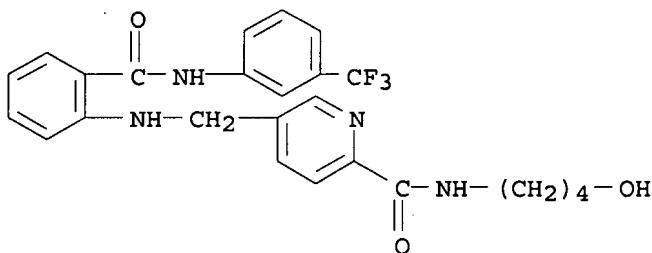
CN 2-Pyridinecarboxamide, N-[(2R)-2-hydroxypropyl]-5-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 474798-90-8 HCPLUS

CN 2-Pyridinecarboxamide, N-(4-hydroxybutyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 10 OF 10 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:658116 HCPLUS

DOCUMENT NUMBER: 137:201332

TITLE: Preparation of heterocyclalkylamine derivatives as remedies for angiogenesis mediated diseases
Chen, Guoqing; Adams, Jeffrey; Bemis, Jean; Booker, Shon; Cai, Guolin; Croghan, Michael; DiPietro, Lucian; Dominguez, Celia; Elbaum, Daniel; Germain, Julie; Geuns-Meyer, Stephanie; Handley, Michael; Huang, Qi; Kim, Joseph L.; Kim, Tae-seong; Kiselyov, Alexander; Ouyang, Xiaohu; Patel, Vinod F.; Smith, Leon M.; Stec, Markian; Tasker, Andrew; Xi, Ning; Xu, Shimin; Yuan, Chester Chenguang

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: PCT Int. Appl., 502 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.

KIND DATE

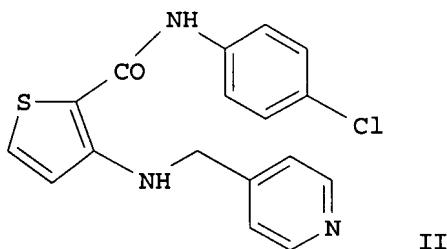
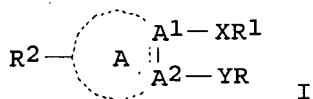
APPLICATION NO.

DATE

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CA 2434277	A1	20020829	CA 2002-2434277	20020111
AU 2002248340	A1	20020904	AU 2002-248340	20020111
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CN 1671700	A	20050921	CN 2002-806202	20020111
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OTHER SOURCE(S):
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MARPAT 137:201332



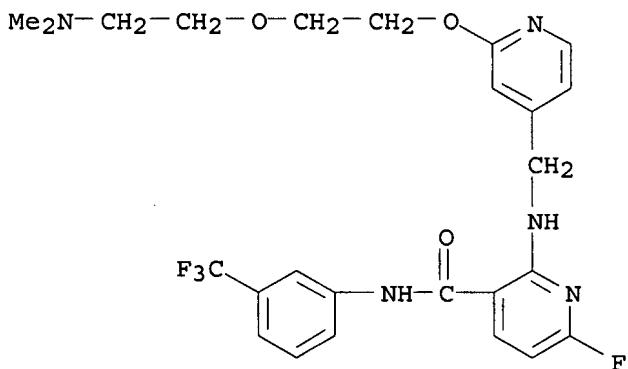
AB Title compds. [I; A1, A2 independently = C, N; A = 5-, or 6-membered partially saturated heterocyclyl, 5-, or 6-membered heterocyclyl, 9-, or 10-membered fused partially saturated heterocyclyl, 9-, 10-, or 11-membered fused heteroaryl, naphthyl, 4-, 5-, or 6-membered cycloalkenyl; X = C:ZNR3, C:ZN(R3)R4; Z = O, S; Y = N:CH, NR5(CR6R7), R8N(R5)(CR6R7), NR5(CR6R7)R8; R = 5-, or 6-membered (un)substituted heterocyclyl, 9-, 10-, 11-membered heterocyclyl; R1 = 6-10-membered (un)substituted aryl, 5-, or 6-membered (un)substituted heterocyclyl, 9-11 membered (un)substituted fused heterocyclyl, cycloalkyl, cycloalkenyl; R2 = H, halo, oxo, SH, COOH, CHO; R3 = H, alkyl, 5-, or 6-membered heterocyclyl; R4 = alkylenyl, alkenylenyl, alkynylenyl; R5 = H, alkyl, aralkyl, C6H5; R6, R7 independently = H, halo, CN, alkyl; R6R7 = cycloalkyl; R8 = alkylenyl; etc.] are prepared and are effective for prophylaxis and treatment of diseases, such as angiogenesis mediated diseases. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable derivs. thereof, pharmaceutical compns. and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like. The subject invention also relates to processes for making such compds. as well as to intermediates useful in such processes. Thus, the title compound II was prepared from Me 3-amino-2-thiophenecarboxylate, 4-chloroaniline, and 4-pyridine carboxaldehyde via coupling reaction.

IT 453563-07-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclylalkylamine derivs. as remedies for angiogenesis mediated diseases)

RN 453563-07-0 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-[2-[2-(dimethylamino)ethoxy]ethoxy]-4-pyridinyl]methyl]amino]-6-fluoro-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



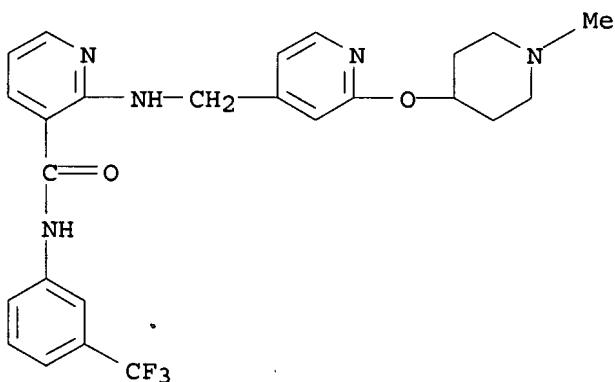
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 453564-81-3P 453564-82-4P 453564-84-6P
 453564-92-6P 453564-93-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclylalkylamine derivs. as remedies for angiogenesis mediated diseases)

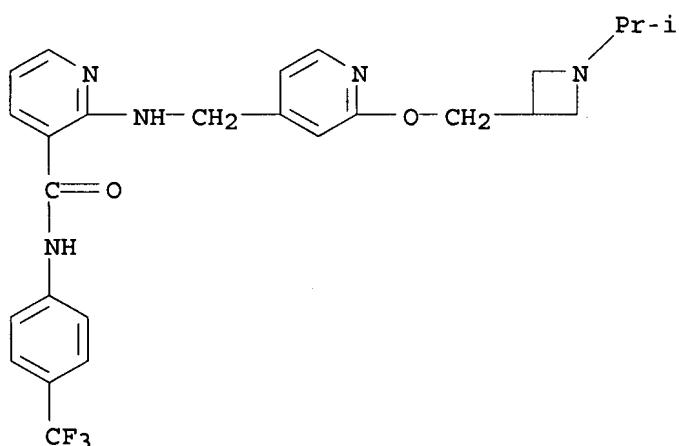
RN 453561-97-2 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[2-[(1-methyl-4-piperidinyl)oxy]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



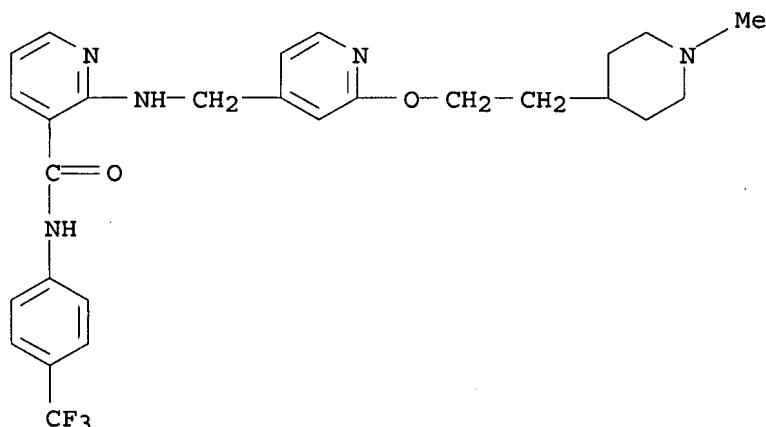
RN 453563-29-6 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[2-[[1-(1-methylethyl)-3-azetidinyl]methoxy]-4-pyridinyl]methyl]amino]-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



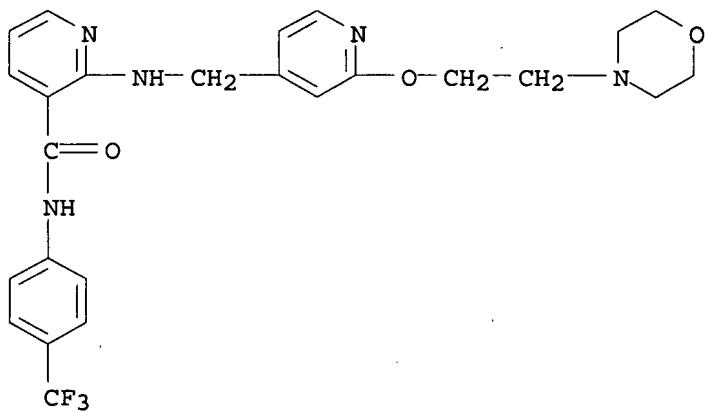
RN 453563-38-7 HCAPLUS

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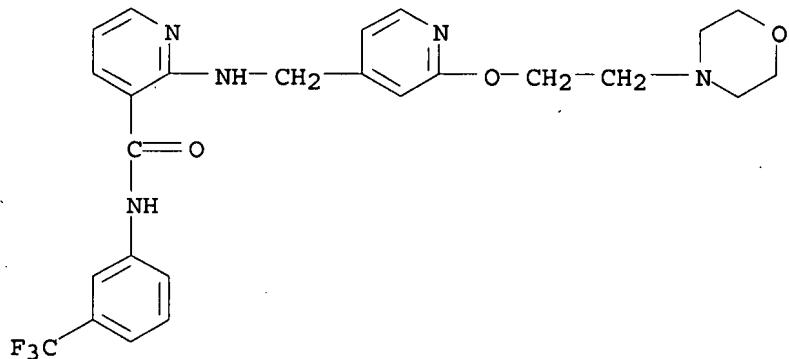
RN 453563-56-9 HCAPLUS

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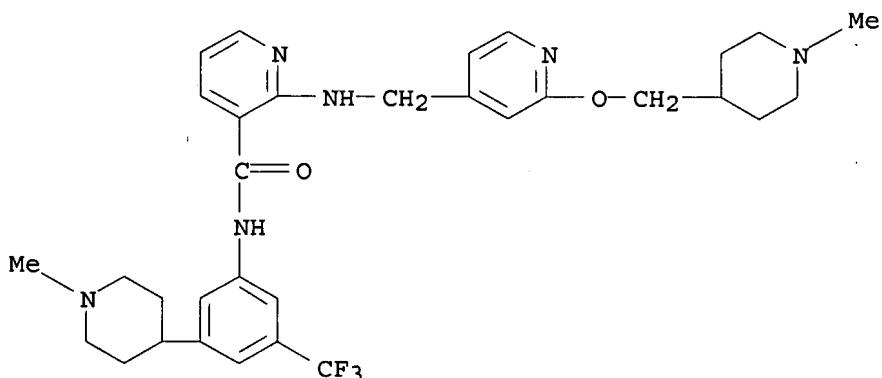
RN 453563-57-0 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-[2-(4-morpholinyl)ethoxy]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 453563-72-9 HCPLUS

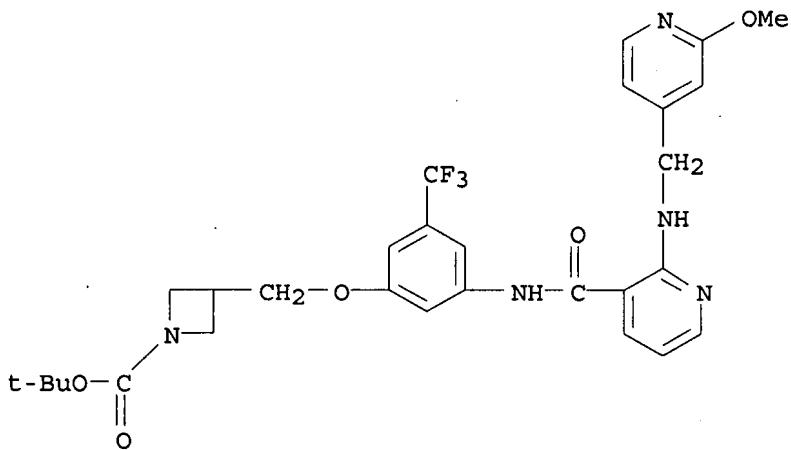
CN 3-Pyridinecarboxamide, 2-[[[2-[(1-methyl-4-piperidinyl)methoxy]-4-pyridinyl]methyl]amino]-N-[3-(1-methyl-4-piperidinyl)-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 453563-75-2 HCPLUS

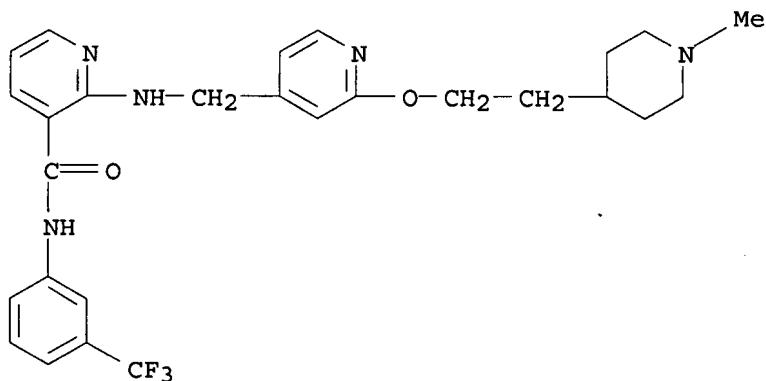
Updated Search

CN 1-Azetidinecarboxylic acid, 3-[[3-[[2-[(2-methoxy-4-pyridinyl)methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenoxy]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



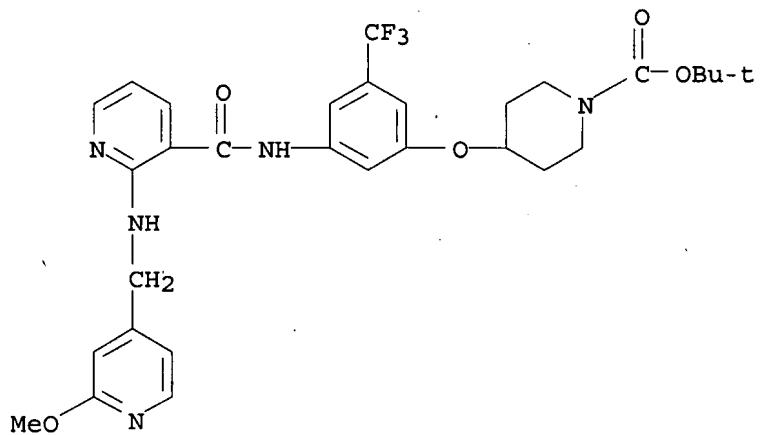
RN 453563-83-2 HCPLUS

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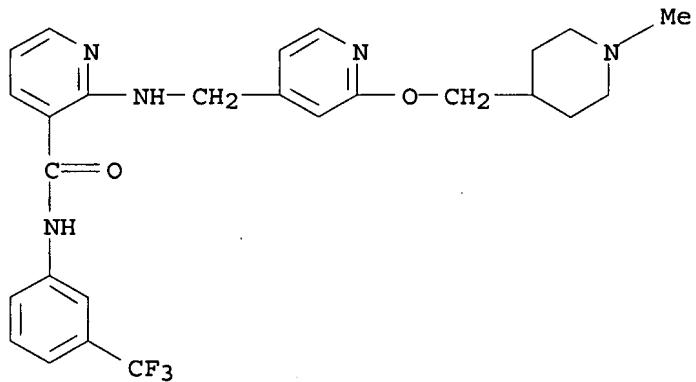
RN 453563-98-9 HCPLUS

CN 1-Piperidinecarboxylic acid, 4-[[3-[[2-[(2-methoxy-4-pyridinyl)methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



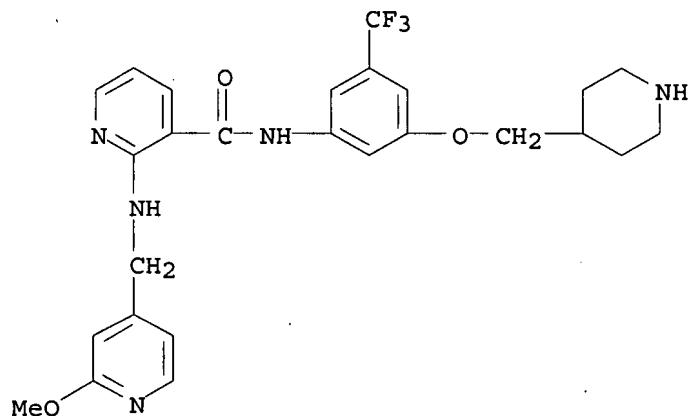
RN 453564-12-0 HCAPLUS

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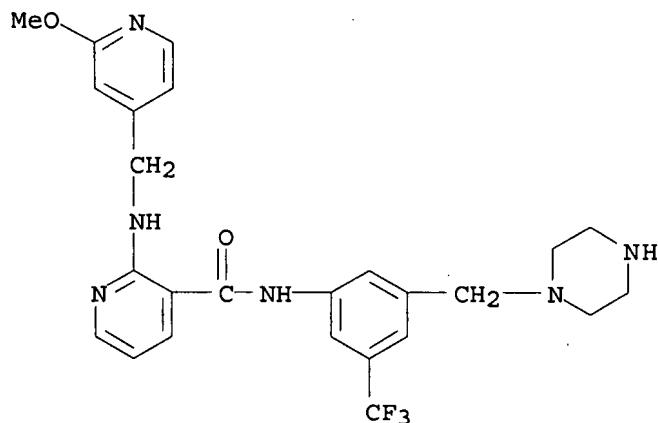
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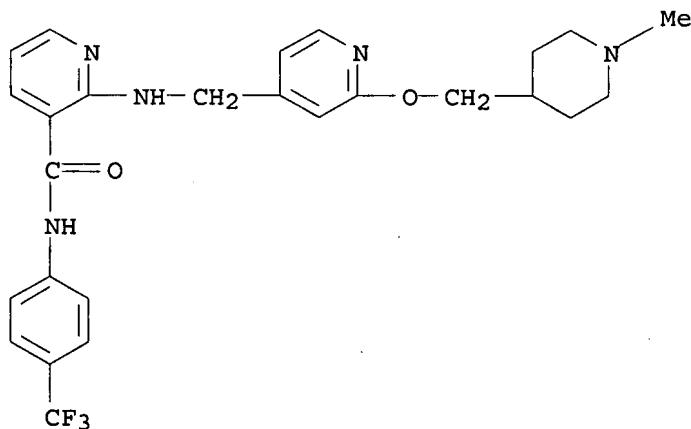
RN 453564-30-2 HCAPLUS

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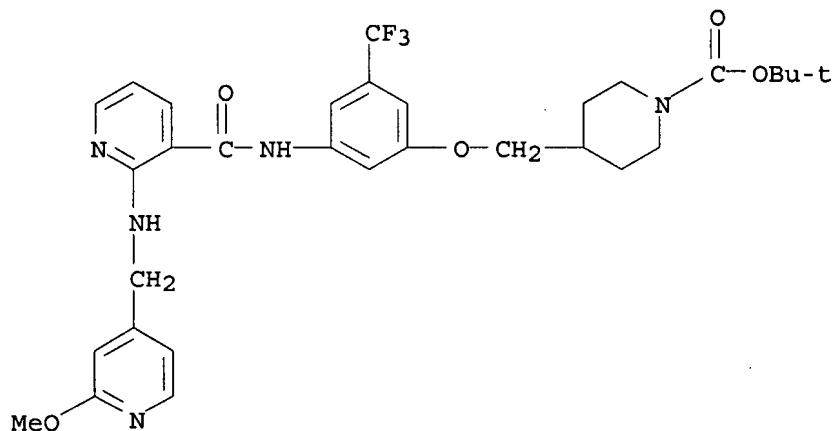
RN 453564-71-1 HCAPLUS

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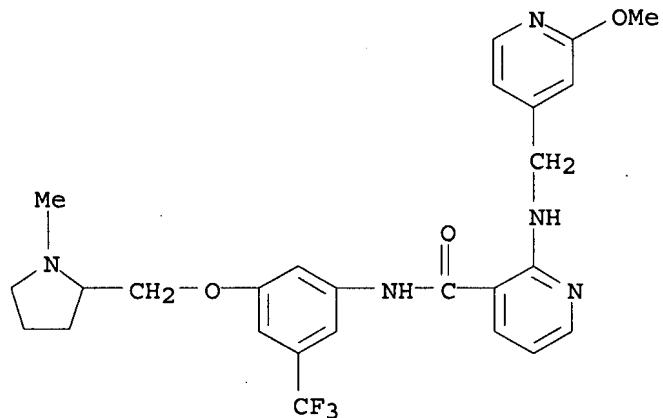
RN 453564-76-6 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[3-[[2-[(2-methoxy-4-pyridinyl)methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenoxy]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



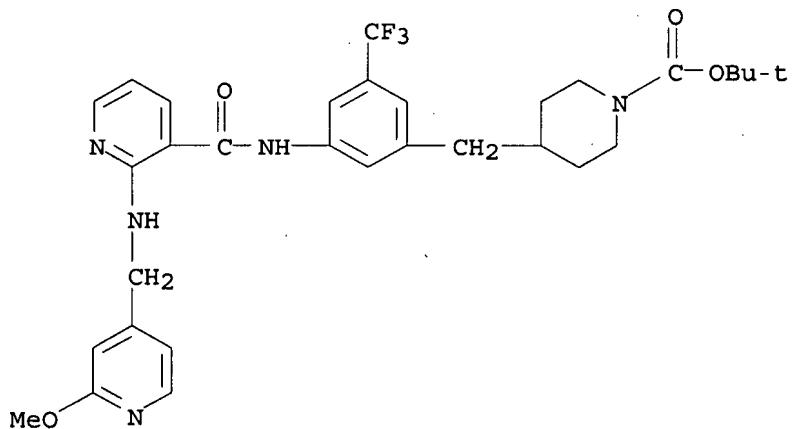
RN 453564-80-2 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[(1-methyl-2-pyrrolidinyl)methoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



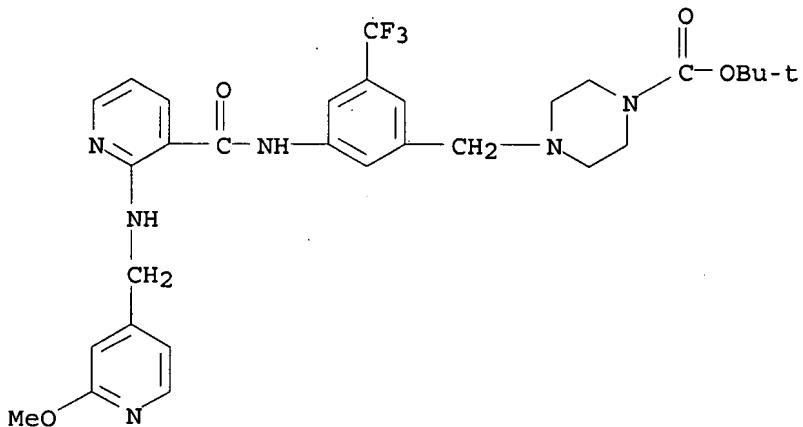
RN 453564-81-3 HCAPLUS

CN 1-Piperidinocarboxylic acid, 4-[[3-[[[2-[(2-methoxy-4-pyridinyl)methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



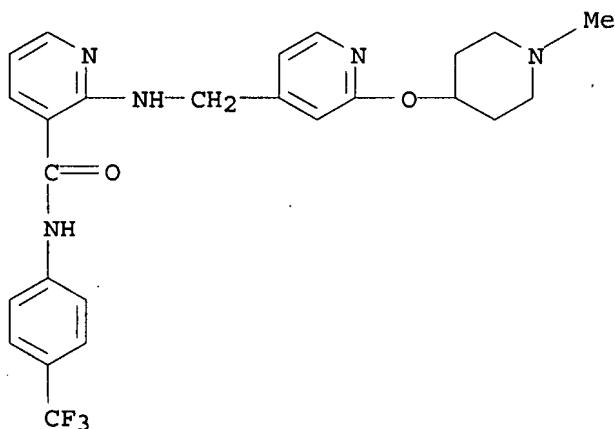
RN 453564-82-4 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[3-[[2-[(2-methoxy-4-pyridinyl)methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



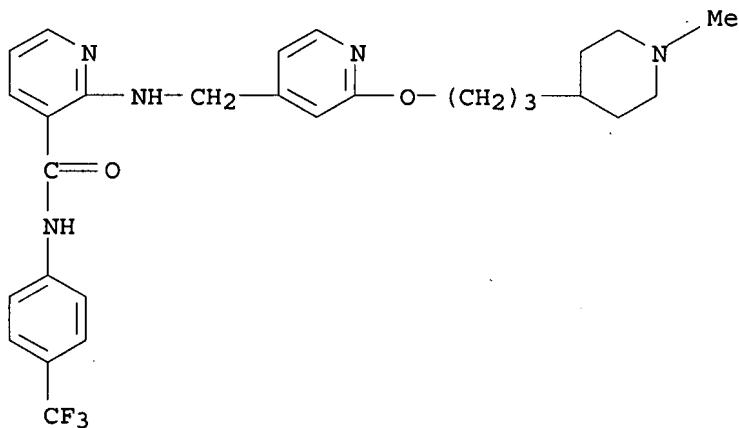
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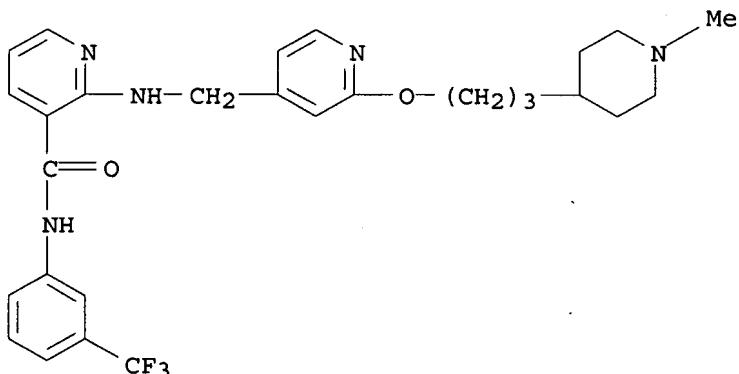
RN 453564-92-6 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[2-[3-(1-methyl-4-piperidinyl)propoxy]-4-pyridinyl]methyl]amino]-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 453564-93-7 HCPLUS

CN 3-Pyridinecarboxamide, 2-[[2-[3-(1-methyl-4-piperidinyl)propoxy]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L7 11 S L5 NOT L6
L8 1 S L7 AND FURET, P?/AU
L9 10 S L7 NOT L8
L10 0 S L9 AND MANLEY, P?/AU

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 FILE LAST UPDATED: 30 Sep 2007 (20070930/ED)

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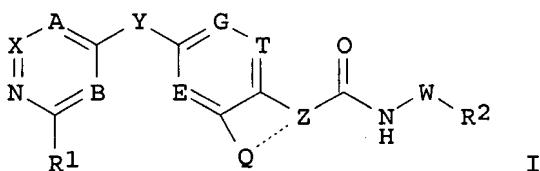
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L12      16 BOLD, G?/AU AND FURET, P?/AU AND MANLEY, P?/AU
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L12 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN .
ACCESSION NUMBER: 2006:538988 HCAPLUS
DOCUMENT NUMBER: 145:46079
TITLE: Preparation of bicyclic amides as kinase inhibitors
INVENTOR(S): Bold, Guido; Capraro, Hans-Georg; Caravatti,
Giorgio; Floersheimer, Andreas; Furet, Pascal
; Manley, Paul W.; Vaupel, Andrea; Pissot
Soldermann, Carole; Gessier, Francois; Schnell,
Christian; Littlewood-Evans, Amanda Jane; Kapa, Prasad
Koteswara; Bajwa, Joginder S.; Jiang, Xinglong
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.M.B.H.
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006059234	A2	20060608	WO 2005-IB4030	20050914
WO 2006059234	A3	20060720		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,			
	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,			

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 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
 NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
 ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 AU 2005310968 A1 20060608 AU 2005-310968 20050914
 CA 2574829 A1 20060608 CA 2005-2574829 20050914
 EP 1794149 A2 20070613 EP 2005-850758 20050914
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR
 CN 101018784 A 20070815 CN 2005-80030767 20050914
 IN 2007DN00915 A 20070803 IN 2007-DN915 20070202
 NO 2007001875 A 20070614 NO 2007-1875 20070413
 PRIORITY APPLN. INFO.: GB 2004-20520 A 20040915
 GI GB 2005-11687 A 20050608
 OTHER SOURCE(S): MARPAT 145:46079 WO 2005-IB4030 W 20050914



AB The invention relates to compds. I [R1 = H, halo, CN, etc.; R2 = substituted cycloalkyl, aryl, heterocyclyl; A, B and X = CR7 or N; E, G and T = CR8 or N; R7, R8 = H, halo, (un)substituted alkyl; Y = O, S, CH2, etc.; Z = CH or N and Q = (un)substituted alkylene or alkenylene (wherein one or more of the carbon atoms may be replaced by a heteroatom selected from N, O or S; and the bond between Q and Z is a single bond; with the proviso that if Z = N, Q is not unsubstituted unbranched alkylene); or Z = C and Q is as defined above wherein the bond between Q and Z characterized by a dotted line is a double bond; W is either not present or alkylene] and their use in the treatment of the animal or human body, to pharmaceutical compns. comprising a compound I and to the use of a compound I for the preparation of pharmaceutical compns. for use in the treatment of protein kinase dependent diseases, especially of proliferative diseases, such

as in particular tumor diseases. Over 100 compds. I were prepared E.g., a 3-step synthesis of rac-5-(2-amino-6-chloropyrimidin-4-yloxy)-4-fluoro-2-methyl-2,3-dihydroindole-1-carboxylic acid (3-trifluoromethylphenyl)amide, starting from 2-amino-4,6-dichloropyrimidine and 4-fluoro-5-hydroxy-2-methylindole, was given.

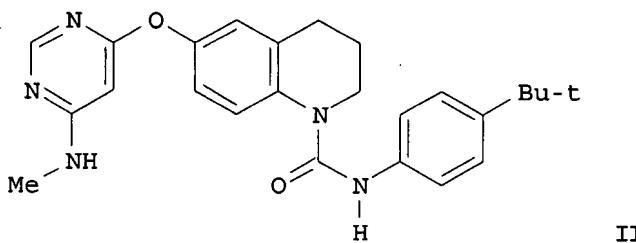
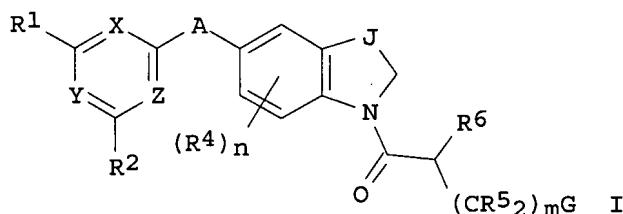
L12 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:318488 HCAPLUS
 DOCUMENT NUMBER: 144:369909
 TITLE: Preparation of cyclic diaryl ureas suitable as tyrosine kinase inhibitors
 INVENTOR(S): Bold, Guido; Caravatti, Giorgio;
 Floersheimer, Andreas; Furet, Pascal;

Manley, Paul W.; Pissot Soldermann, Carole;
 Vaupel, Andrea
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
 SOURCE: PCT Int. Appl., 140 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006034833	A1	20060406	WO 2005-EP10408	20050927
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005289136	A1	20060406	AU 2005-289136	20050927
CA 2577185	A1	20060406	CA 2005-2577185	20050927
EP 1807412	A1	20070718	EP 2005-796941	20050927
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101031560	A	20070905	CN 2005-80032726	20050927
IN 2007DN01701	A	20070817	IN 2007-DN1701	20070302
PRIORITY APPLN. INFO.:			GB 2004-21525	A 20040928
			WO 2005-EP10408	W 20050927

OTHER SOURCE(S): CASREACT 144:369909; MARPAT 144:369909
 GI



AB Title compds. I [A = S, O, CH₂, etc.; X, Y and Z independently = N or CR₃ wherein at least two of X, Y and Z = N; R₁₋₃ independently = halo, OH, alkyl, etc.; R₄ = halo, OH, alkyl, mercapto, etc.; R₅₋₇ independently = H or alkyl; G = CN or (un)substituted 5-6 membered monocyclic or 8-12 membered bicyclic or tricyclic ring which may contain 0-3 heteroatoms and be optionally saturated or unsatd.; J = (CR₂)_p; wherein m, n or p independently = 0-3] and their pharmaceutically acceptable salts, esters, N-oxides or prodrugs thereof are prepared and disclosed for the use in the treatment of protein kinase dependent diseases. Thus, e.g., II was prepared by reaction of 6-methylamino-4-(1,2,3,4-tetrahydroquinolin-6-yloxy)pyrimidine (preparation given) with 4-tert-butylphenylisocyanate. Assays are described for determining activity of I as kinase inhibitors (no data). Specific tyrosine kinases identified as associated with a proliferative condition include ras, Abl, VEGF-receptor tyrosine kinase, Flt3, Bcr-Abl receptors, and substitution mutants of Bcr-Abl. Further disclosed are claims to the use of I in the manufacture of pharmaceutical compns. for use in the treatment of said diseases, methods of use of diaryl urea derivs. in the treatment of said diseases, pharmaceutical preps. comprising these novel diaryl urea derivs., processes for the manufacture of the novel diaryl urea derivs., the use or methods of use of the novel diaryl urea derivs. as mentioned above, and/or these novel diaryl urea derivs. for use in the treatment of the animal or human body.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:15086 HCAPLUS

DOCUMENT NUMBER: 144:108347

TITLE: Preparation of pyrimidine urea derivatives as kinase inhibitors for use against proliferative diseases

INVENTOR(S): Ding, Qiang; Gray, Nathanael Schiander; Li, Bing; Liu, Yi; Sim, Taebo; Uno, Tetsuo; Zhang, Guobao; Pissot Soldermann, Carole; Breitenstein, Werner; Bold, Guido; Caravatti, Giorgio; Furet, Pascal ; Guagnano, Vito; Lang, Marc; Manley, Paul W. ; Schoepfer, Joseph; Spanka, Carsten

PATENT ASSIGNEE(S): Novartis AG, Switz.

SOURCE: PCT Int. Appl., 327 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

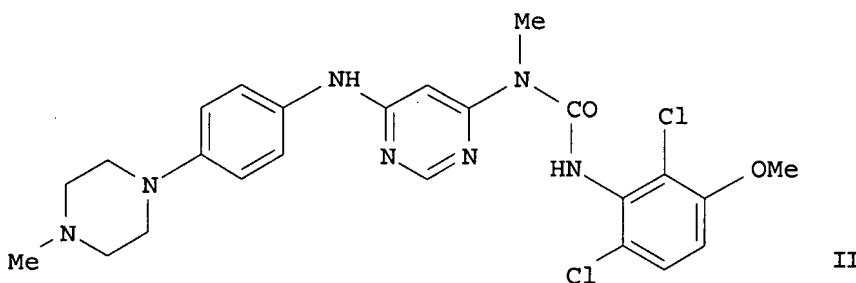
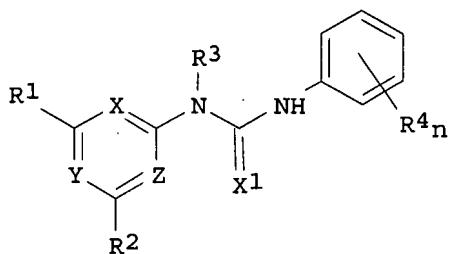
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006000420	A1	20060105	WO 2005-EP6815	20050623
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005256491	A1	20060105	AU 2005-256491	20050623
CA 2570873	A1	20060105	CA 2005-2570873	20050623

EP 1761505	A1	20070314	EP 2005-756693	20050623
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LV				
CN 101035769	A	20070912	CN 2005-80024896	20050623
IN 2006DN06843	A	20070831	IN 2006-DN6843	20061116
NO 2007000432	A	20070326	NO 2007-432	20070123
PRIORITY APPLN. INFO.:			US 2004-582425P	P 20040624
GI			GB 2005-12324	A 20050616
OTHER SOURCE(S):	MARPAT 144:108347		WO 2005-EP6815	W 20050623

OTHER SOURCE(S): MARPAT 144:108347
GI



AB The invention relates to pyrimidine urea derivs. (shown as I; variables defined below; e.g. 3-(2,6-dichloro-3-methoxyphenyl)-1-methyl-1-[6-[[4-(4-methylpiperazin-1-yl)phenyl]amino]pyrimidin-4-yl]urea (II)), to processes for the preparation of these compds., pharmaceutical compns. containing same,

the

use thereof optionally in combination with ≥1 other pharmaceutically active compds. for the therapy of a disease which responds to an inhibition of protein kinase activity, and a method for the treatment of such a disease. Inhibitory activity of some examples of I are included, e.g. N-[3-[3-(6-aminopyrimidin-4-yl)-3-[3-(2-oxopyrrolidin-1-yl)propyl]ureido]-4-methylphenyl]-3-trifluoromethylbenzamide at a concentration of 10 μM inhibits the following kinases by the percentage shown in brackets: wild-type Abl (99%), c-RAF (99%), CSK (97%), c-SRC (100%), FGFR35 (99%), JNK2α2 (93%), lck (100%), MKK6 (88%), p70S6K (81%), ROS (95%), SAPK2α (99%), SAPK2β (99%), Tie2 (100%) and TrkB (99%). For I: n = 0-5; X, Y and Z = N or CR5, wherein at least two of X, Y and Z are N; X1 is O; R1, R2, R3 and R4, if present, = an organic or inorg. moiety, where the inorg. moiety especially = halo, especially chloro, hydroxy, cyano, azido, nitro; and where the organic moiety is (un)substituted and may be attached via a linker, -L1-, the organic moiety especially = H lower aliphatic, amino, guanidino, hydroxyguanidino, formamidino, isothioureido, et al. and -L1-

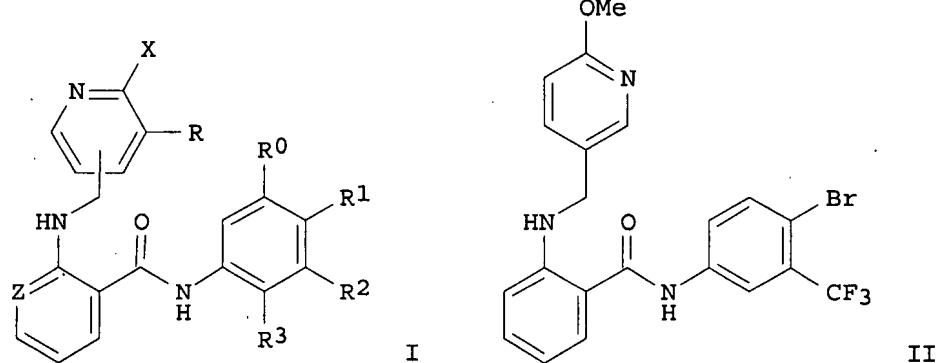
has 1-5 in-chain atoms (e.g. = C, N, O and S) and optionally = (i) C1-C4 alkyl, such an alkyl group optionally being interrupted and/ or terminated by an -O-, -C(O)- or -NRA- linkage, -O-, -S-, -C(O)-, cyclopropyl (regarded as having two in-chain atoms) and chemical appropriate combinations thereof. R1 can also = -X5NR7R8, -X5NR7X5NR7R8, -X5NR7X5C(O)OR8, -X5OR7, -X5R7 and -X5S(O)0-2R7 (X5 is a bond or (un)substituted C1-4alkylene; R7 = H, C1-6alkyl, C6-10aryl-C0-4alkyl, C5-10heteroaryl-C0-4alkyl, C3-10cycloalkyl-C0-4alkyl and C3-10heterocycloalkyl-C0-4alkyl; and R8 = H and C1-6alkyl; or R7 and R8 together with the N to which R7 and R8 are both attached form heteroaryl or heterocycloalkyl); wherein R3 can alternatively = H, C1-4alkyl, C6-10aryl-C0-4alkyl, C5-10heteroaryl-C0-4alkyl, C3-10cycloalkyl-C0-4alkyl and C3-10heterocycloalkyl-C0-4alkyl. Each R4 is the same or different and = an organic or inorg. moiety, e.g. halogen, hydroxy, protected hydroxy; one of the R4 can also = -L1-A-R16m (L1 is a linker; m is 0-5; A is a ring; R16, if present, = an organic or inorg. moiety, where the inorg. moiety especially = halo, especially chloro, hydroxy, cyano, azido, nitro; and where the organic moiety is (un)substituted and may be attached via a linker, -L2-, the organic moiety being especially = H, lower aliphatic (especially C1-C4 aliphatic), et al.; L1 and L2 each independently = moieties having 1-5 in-chain atoms (e.g. = C, N, O and S) and optionally being = C1-C4 alkyl, such an alkyl group optionally being interrupted and/or terminated by an -O-, -C(O)- or -NRA- linkage, -O-, -S-, -C(O)-, cyclopropyl (regarded as having two in-chain atoms) and chemical appropriate combinations thereof; addnl. details including provisos are given in the claims. Although the methods of preparation are not claimed, prepns. and/or characterization data for >200 examples of I are included. For example, II was prepared from 2,6-dichloro-3-methoxyphenyl isocyanate (preparation given) and N-methyl-N'-(4-(4-methylpiperazin-1-yl)phenyl)pyrimidine-4,6-diamine (preparation given).

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 16 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:515506 HCPLUS
 DOCUMENT NUMBER: 141:71453
 TITLE: Preparation of anthranilic acid amide derivatives as neoplastic inhibitors
 INVENTOR(S): Bold, Guido; Furet, Pascal;
 Manley, Paul William
 PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH
 SOURCE: PCT Int. Appl., 81 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052884	A1	20040624	WO 2003-EP14086	20031211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,				

DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
 SI, SK, TR
 CA 2506164 A1 20040624 CA 2003-2506164 20031211
 AU 2003294834 A1 20040630 AU 2003-294834 20031211
 EP 1572686 A1 20050914 EP 2003-785795 20031211
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 BR 2003017292 A 20051108 BR 2003-17292 20031211
 CN 1720244 A 20060111 CN 2003-80104845 20031211
 JP 2006511518 T 20060406 JP 2004-558075 20031211
 US 2006128684 A1 20060615 US 2005-538199 20050609
 PRIORITY APPLN. INFO.: GB 2002-29022 A 20021212
 OTHER SOURCE(S): MARPAT 141:71453 W 20031211
 GI



AB The title compds. I [wherein R and R0 = independently H, halo, (un)substituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, etc.; R1 = H, halo, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, OCF₃, OCH₂CF₃, OCH₂CH₂CF₃, or OCH₂CH₂CH₂CF₃; R2 = perfluoroalkyl; R3 = H or halo; X = OH, alkoxy, alkylthio, imino, alkylimino, halo, etc.; Z = N or CH] or salts, N-oxides, or tautomers thereof are prepared as neoplastic inhibitors for the treatment of human or animal body. For example, the compound II was prepared in a multi-step synthesis. Formulations containing I as an active ingredient were also described.

L12 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:216609 HCAPLUS
 DOCUMENT NUMBER: 140:417028
 TITLE: Advances in the structural biology, design and clinical development of VEGF-R kinase inhibitors for the treatment of angiogenesis
 AUTHOR(S): Manley, Paul William; Bold, Guido;
 Brueggen, Josef; Fendrich, Gabrielle; Furet, Pascal;
 Mestan, Jurgen; Schnell, Christian;
 Stoltz, Barbara; Meyer, Thomas; Meyhack, Bernd; Stark, Wilhelm;
 Strauss, Andre; Wood, Jeanette
 CORPORATE SOURCE: Novartis Institutes of Biomedical Research, Basel,
 CH-4002, Switz.
 SOURCE: Biochimica et Biophysica Acta, Proteins and Proteomics (2004), 1697(1-2), 17-27
 CODEN: BBAPBW; ISSN: 1570-9639
 PUBLISHER: Elsevier B.V.
 DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Initial studies with angiogenesis inhibitors showed little clin. benefit. However, recently reported clin. studies in colorectal cancer have shown that bevacizumab, a vascular endothelial growth factor (VEGF) monoclonal antibody, in combination with cytotoxic therapy has pos. effects on patient survival. Furthermore, the VEGF receptor kinase (VEGF-R) tyrosine kinase inhibitor, vatalanib, has also shown encouraging results in colorectal cancer, with mol. resonance imaging providing evidence that the anti-tumor efficacy was indeed the result of anti-angiogenic activity. Both of these agents are progressing in phase III trials. This proof of concept has stimulated the desire for second-generation VEGF-R inhibitors having an improved profile. Structural biol. insight regarding the binding mode of protein kinase inhibitors is valuable for the design of mols. possessing superior selectivity, efficacy and tolerability. Towards this goal, the authors have developed a new series of VEGF-R2 kinase inhibitors, based upon an anthranilic acid amide scaffold. An x-ray crystal structure of a representative compound, AAL993 (ZK260253), in complex with the catalytic domain of diphosphorylated VEGF-R2 has revealed that this mol. binds to an inactive conformation of the protein. This binding mode, similar to that observed for the anti-leukemia drug, imatinib in complex with c-Abl kinase, may be responsible for the high selectivity of AAL993 and provides valuable insight for the design of further compds.

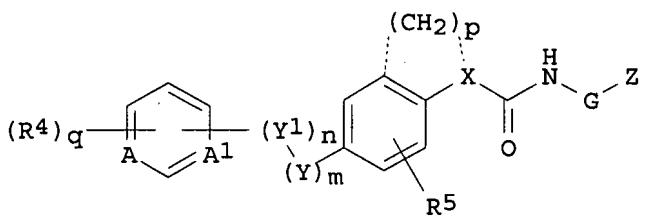
REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:950982 HCAPLUS
 DOCUMENT NUMBER: 140:16736
 TITLE: Preparation of diarylurea derivatives useful for the treatment of protein kinase dependent diseases
 INVENTOR(S): Floersheimer, Andreas; Furet, Pascal;
 Manley, Paul William; Bold, Guido;
 Boss, Eugen; Guagnano, Vito; Vaupel, Andrea
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
 SOURCE: PCT Int. Appl., 170 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099771	A2	20031204	WO 2003-EP5634	20030528
WO 2003099771	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2484288	A1	20031204	CA 2003-2484288	20030528
AU 2003242591	A1	20031212	AU 2003-242591	20030528
AU 2003242591	B2	20070726		
BR 2003011313	A	20050215	BR 2003-11313	20030528
EP 1511730	A2	20050309	EP 2003-755147	20030528
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CN 1656073	A	20050817	CN 2003-812280	20030528
JP 2005527622	T	20050915	JP 2004-507429	20030528
ZA 2004008314	A	20060726	ZA 2004-8314	20041014
IN 2004CN02670	A	20070720	IN 2004-CN2670	20041125
MX 2004PA11789	A	20050331	MX 2004-PA11789	20041126
NO 2004005521	A	20041217	NO 2004-5521	20041217
US 2006128734	A1	20060615	US 2005-515113	20051208
PRIORITY APPLN. INFO.:			GB 2002-12413	A 20020529
			GB 2003-5684	A 20030312
			GB 2003-9219	A 20030423
			WO 2003-EP5634	W 20030528

OTHER SOURCE(S): MARPAT 140:16736
GI



AB The invention relates to the use of diaryl urea derivs. [I; G is not present and Z = a radical of the formula Q; A = CH, N, N⁺O; A1 = N, N⁺O, with the proviso that not more than one of A and A1 can be N⁺O; n = 1, 2; m = 0-2; p = 0, 2, 3; q = 0-5; X = (un)substituted NH if p = 0; or if p is 2 or 3, X = nitrogen which together with (CH2)p and the bonds represented in dotted (interrupted) lines (including the atoms to which they are bound) forms a ring, or X = CHK (wherein K = H or lower alkyl) and p = 0, with the proviso that the bonds represented in dotted lines, if p = 0, are absent; Y1 = O, S, CH2; Y2 = O, S, NH; with the proviso that (Y1)n-(Y2)m does not include O-O, S-S, NH-O, NH-S or S-O groups; R1, R2, R3, R5 = independently H or an inorg. or organic moiety or any two of them together form a lower alkyleneoxy bridge bound via the oxygen atoms, and the remaining one of these moieties is hydrogen or an inorg. or organic moiety; R4 (if present, i.e., if q is not zero) is an inorg. or organic moiety] or tautomers thereof or pharmaceutically acceptable salts thereof in the treatment of protein kinase dependent diseases or for the manufacture of pharmaceutical compns. for use in the treatment of said diseases, especially a proliferative disease depending on any one or more of

the

following (tyrosine) protein kinases such as ras, Ab1, VEGF-receptor tyrosine kinase, Flt3, and/or Bcr-Ab1 activity. Also disclosed are the use of the compds. I for the manufacture of pharmaceutical compns. for use in the treatment of said diseases, methods of use of the compds. I in the treatment of said diseases, pharmaceutical prepns. comprising the compds. I for the treatment of said diseases, processes for the manufacture of the compds. I, the use or methods of use of the compds. I as mentioned above, and/or the compds. I for use in the treatment of the animal or human body. For example, N-(4-(pyridin-4-yloxy)phenyl)-N'-(4-2,2,2-trifluoroethoxy-3-trifluoromethylphenyl)urea and N-[4-[6-(4-hydroxyphenylamino)pyrimidin-4-yl]phenyl]-N'-(4-2,2,2-trifluoroethoxy-3-trifluoromethylphenyl)urea at 10 μM inhibited gene c-Ab1 protein kinase by 98%, Kdr receptor tyrosine kinase by 100 and 96%, resp., and Flt3 receptor tyrosine kinase by 100%.

L12 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:665525 HCAPLUS

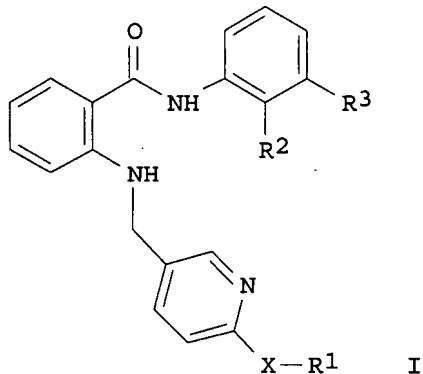
DOCUMENT NUMBER: 139:345320
 TITLE: Identification of a new chemical class of potent angiogenesis inhibitors based on conformational considerations and database searching
 AUTHOR(S): Furet, Pascal; Bold, Guido;
 Hofmann, Francesco; Manley, Paul; Meyer, Thomas; Altmann, Karl-Heinz
 CORPORATE SOURCE: Oncology Research, Novartis Pharma AG, Basel, CH-4002, Switz.
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(18), 2967-2971
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 139:345320
AB The vascular endothelial growth factor (VEGF) tyrosine kinase receptors KDR and Flt-1 are targets of current interest in anticancer drug research. PTK787/ZK222584 is a potent inhibitor of these enzymes in clin. evaluation as an antiangiogenic agent. The development of a hypothesis concerning the bioactive conformation of this compound has led to the discovery of a new class of potent inhibitors of KDR and Flt-1, the anthranilamides. This could be achieved with a limited exptl. effort, which only involved the testing of one archive compound and the synthesis and testing of one appropriate analog.
 REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 16 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:376825 HCPLUS
 DOCUMENT NUMBER: 138:385308
 TITLE: Preparation of anthranilic acid amides and their use as vascular endothelial growth factor receptor tyrosine kinase inhibitors
 INVENTOR(S): Bold, Guido; Furet, Pascal;
 Manley, Paul William
 PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040102	A1	20030515	WO 2002-EP12444	20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
TW 260222	B	20060821	TW 2002-91132669	20021106
CA 2463968	A1	20030515	CA 2002-2463968	20021107
AU 2002351909	A1	20030519	AU 2002-351909	20021107
AU 2002351909	B2	20070426		
EP 1446382	A1	20040818	EP 2002-787595	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

BR 2002013970	A	20040831	BR 2002-13970	20021107
CN 1585750	A	20050223	CN 2002-822209	20021107
JP 2005511602	T	20050428	JP 2003-542148	20021107
NZ 532590	A	20051223	NZ 2002-532590	20021107
ZA 2004002940	A	20050210	ZA 2004-2940	20040419
US 2005096356	A1	20050505	US 2004-494591	20040505
US 7091224	B2	20060815		
IN 2004CN00972	A	20060203	IN 2004-CN972	20040506
NO 2004002187	A	20040526	NO 2004-2187	20040526
US 2006178409	A1	20060810	US 2006-374720	20060314
PRIORITY APPLN. INFO.:			GB 2001-26902	A 20011108
			WO 2002-EP12444	W 20021107
			US 2004-494591	A1 20040505

OTHER SOURCE(S): MARPAT 138:385308
GI



AB Anthranilic acid amide derivs. [I; R1, R2 = H, lower alkyl; R3 = lower perfluoroalkyl; X = O, S; e.g., 2-[(6-Methoxy-3-pyridinyl)methyl]amino-N-[3-(trifluoromethyl)phenyl]benzamide hydrochloride, m.p. 133-135°], which are vascular endothelial growth factor receptor tyrosine kinase inhibitors for the treatment of neoplastic disease, of retinopathy or age-related macular degeneration, are prepared and a I-containing formulation presented (e.g., a soft capsule).

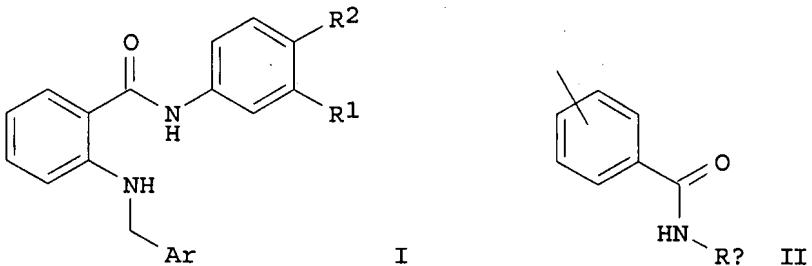
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 16 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:376824 HCPLUS
 DOCUMENT NUMBER: 138:368777
 TITLE: Preparation of pyridyl-substituted anthranilic acid amides for treating neoplastic disease
 INVENTOR(S): Bold, Guido; Furet, Pascal;
 Manley, Paul William
 PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH
 SOURCE: PCT Int. Appl., 33 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO	2003040101	A1	20030515	WO	2002-EP12445	20021107
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW					
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR					
TW	260985	B	20060901	TW	2002-91132668	20021106
CA	2462390	A1	20030515	CA	2002-2462390	20021107
AU	2002342889	A1	20030519	AU	2002-342889	20021107
AU	2002342889	B2	20070301			
EP	1446381	A1	20040818	EP	2002-779536	20021107
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR	2002013939	A	20040831	BR	2002-13939	20021107
CN	1578768	A	20050209	CN	2002-821430	20021107
JP	2005508382	T	20050331	JP	2003-542147	20021107
NZ	532587	A	20060224	NZ	2002-532587	20021107
NZ	543915	A	20070629	NZ	2002-543915	20021107
US	2004248947	A1	20041209	US	2004-494222	20040503
US	7067543	B2	20060627			
IN	2004CN00973	A	20060203	IN	2004-CN973	20040506
MX	2004PA04390	A	20050516	MX	2004-PA4390	20040507
NO	2004002137	A	20040525	NO	2004-2137	20040525
ZA	200402623	A	20060531	ZA	2004-2623	20060328
RITY APPLN. INFO.:				GB	2001-26901	A 20011108
				GB	2002-12917	A 20020605
				NZ	2002-532587	A3 20021107
				WO	2002-EP12445	W 20021107

OTHER SOURCE(S) : MARPAT 138:368777
GI

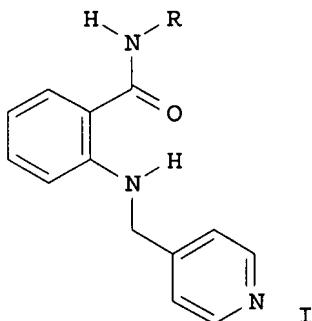


AB The title compds. [I; Ar = II (wherein Ra = H, alkyl; and R1 = H, perfluoroalkyl; R2 = H, halo, alkyl, alkenyl, alkynyl); or Ar = 4-pyridyl and R1 = perfluoroalkyl; R2 = Br, I, alkyl, alkenyl, alkynyl; or R1 = H, and R2 = F, Br, I, Et, alkyl, alkenyl or alkynyl] and their N-oxides and salts, useful for the treatment especially of a neoplastic disease, such as a tumor disease, of retinopathy or age-related macular degeneration in the human or animal body, were prepared and formulated. Thus, reductive amination of 4-pyridinecarboxaldehyde with 2-amino-N-(4-bromo-3-trifluoromethylphenyl)benzamide (preparation given) in the presence of NaBH3CN afforded I [Ar = 4-pyridyl; R1 = CF₃; R2 = Br]. The IC₅₀-values that can be found for the compds. I are in range of 0.001 to 1 μM in test for activity against VEGF-receptor tyrosine kinase.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:880425 HCAPLUS
DOCUMENT NUMBER: 138:106488
TITLE: Anthranilic Acid Amides: A Novel Class of
Antiangiogenic VEGF Receptor Kinase Inhibitors
AUTHOR(S): Manley, Paul W.; Furet, Pascal;
Bold, Guido; Brueggen, Josef; Mestan, Juergen;
Meyer, Thomas; Schnell, Christian R.; Wood, Jeanette;
Haberey, Martin; Huth, Andreas; Krueger, Martin;
Menrad, Andreas; Ottow, Eckhard; Seidelmann, Dieter;
Siemeister, Gerhard; Thierauch, Karl-Heinz
CORPORATE SOURCE: Oncology Research, Novartis Pharma AG, Basel, CH-4057,
Switz.
SOURCE: Journal of Medicinal Chemistry (2002), 45(26),
5687-5693
PUBLISHER: CODEN: JMCMAR; ISSN: 0022-2623
American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:106488
GI



AB Two readily synthesized anthranilamide, VEGF receptor tyrosine kinase inhibitors have been prepared and evaluated as angiogenesis inhibitors. 2-[(4-Pyridyl)methyl]amino-N-[3-(trifluoromethyl)phenyl]benzamide [I; R = 3-CF₃C₆H₄ (II)] and N-3-isoquinolinyl-2-[(4-pyridinylmethyl)amino]benzamide [I; R = 3-isoquinolinyl (III)] potently and selectively inhibit recombinant VEGFR-2 and VEGFR-3 kinases. As a consequence of their physicochem. properties, these anthranilamides readily penetrate cells and are absorbed following once daily oral administration to mice. Both II and III potently inhibit VEGF-induced angiogenesis in an implant model, with ED₅₀ values of 7 mg/kg. In a mouse orthotopic model of melanoma, II and III potently inhibited both the growth of the primary tumor as well as the formation of spontaneous peripheral metastases. The anthranilamides II and III represent a new structural class of VEGFR kinase inhibitors, which possess potent antiangiogenic and antitumor properties.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:304375 HCAPLUS

DOCUMENT NUMBER: 138:49187
TITLE: CGP 79787D (PTK787/ZK222584), CGP 84738, NVP-AAC789,
NVP-AAD777, and related 1-anilino-(4-pyridylmethyl)phthalazines as inhibitors of VEGF- and
bFGF-induced angiogenesis
AUTHOR(S): Bold, Guido; Frei, Jorg; Furet, Pascal; Manley, Paul W.; Bruggen, Josef; Cozens, Robert; Ferrari, Stefano; Hofmann, Francesco; Martiny-Baron, Georg; Mestan, Jurgen; Meyer, Thomas; Wood, Jeanette M.
CORPORATE SOURCE: Oncology Research, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Drugs of the Future (2002), 27(1), 43-55
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The pharmacol. profile of the class of 1-anilino-(4-pyridylmethyl)-phthalazines is presented. 1-Anilino-(4-pyridylmethyl)phthalazines are potent, selective and orally well absorbed inhibitors of vascular endothelial growth factor (VEGF) receptor tyrosine kinases. In vitro they block VEGF-stimulated autophosphorylation of KDR expressing cells, resulting in the inhibition of survival effects of VEGF on endothelial cells. They also block platelet derived factor-mediated effects at slightly higher concentration but do not affect other pathways such as the bFGF receptor.
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 16 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:803259 HCPLUS
DOCUMENT NUMBER: 137:15067
TITLE: Tyrosine kinase inhibitors: From rational design to clinical trials
AUTHOR(S): Traxler, Peter; Bold, Guido; Buchdunger, Elisabeth; Caravatti, Giorgio; Furet, Pascal; Manley, Paul; O'Reilly, Terence; Wood, Jeanette; Zimmermann, Juerg
CORPORATE SOURCE: Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Medicinal Research Reviews (2001), 21(6), 499-512
CODEN: MRREDD; ISSN: 0198-6325
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Protein kinases play a crucial role in signal transduction as well as in cellular proliferation, differentiation, and various regulatory mechanisms. The inhibition of growth related kinases, especially Tyr kinases, might provide new therapies for diseases such as cancer. The progress made in the crystallization of protein kinases has confirmed that the ATP-binding domain of Tyr kinases is an attractive target for drug design. Three successful examples of drug design at Novartis using a Tyr kinase as a mol. target are described. PK1166, a pyrrolo[2,3,-d]pyrimidine derivative, is a dual inhibitor of both the EGFR and the ErbB2 kinases. The compound entered clin. trials in 1999, based on its favorable pre-clin. profile: potent inhibition of EGF-mediated signalling in cells, in vivo antitumor activity in several EGFR over-expressing xenograft tumor models in nude mice, long-lasting inhibition of EGF-stimulated EGFR auto-phosphorylation in tumor tissue, good oral bioavailability in animals, and no prohibitive in vitro and in vivo toxicity findings. The anilino-phthalazine derivative

PTK787/ZK222584 (Phase I, co-developed by Schering AG, Berlin) is a potent and selective inhibitor of both the KDR and Flt-1 kinases with interesting anti-angiogenic and pharmacokinetic properties (orally bioavailable). STI 571 (Glivec, Gleevec), a phenylamino-pyrimidine derivative, is a potent inhibitor of the Abl Tyr kinase, which is present in 95% of patients with chronic myelogenous leukemia (CML). The compound specifically inhibits proliferation of v-Abl and Bcr-Abl expressing cells (including cells from CML patients) and shows anti-tumor activity as a single agent in animal models at well-tolerated doses. Pharmacol. relevant concns. are achieved in the plasma of animals (oral administration). Promising data from phase I and II clin. trials in CML patients (98% hematol. response rate in Phase I) support the fact that the STI571 represents a new treatment modality for CML. In addition, potent inhibition of the PDGFR and c-Kit Tyr kinases also indicates its possible clin. use in solid tumors.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 16 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:509389 HCPLUS

DOCUMENT NUMBER: 134:216785

TITLE: New anilinophthalazines as potent and orally well absorbed inhibitors of the VEGF receptor tyrosine kinases useful as antagonists of tumor-driven angiogenesis. [Erratum to document cited in CA133:99079]

AUTHOR(S): Bold, Guido; Altmann, Karl-Heinz; Frei, Joerg; Lang, Marc; Manley, Paul W.; Traxler, Peter; Wietfeld, Bernhard; Brueggen, Josef; Buchdunger, Elisabeth; Cozens, Robert; Ferrari, Stefano; Furet, Pascal; Hofmann, Francesco; Martiny-Baron, Georg; Mestan, Juergen; Roesel, Johannes; Sills, Matthew; Stover, David; Acemoglu, Figan; Boss, Eugen; Emmenegger, Rene; Laesser, Laurent; Masso, Elvira; Roth, Rosemarie; Schlachter, Christian; Vetterli, Werner; Wyss, Dominique; Wood, Jeanette M.

CORPORATE SOURCE: Oncology Research and Process Research, NOVARTIS Pharma AG, Basel, CH-4002, Switz.

SOURCE: Journal of Medicinal Chemistry (2000), 43(16), 3200
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB On page 2316, in Table 3, the unit for cmax; the concentration should be given as

[μ M]. The correct version of Table 3 is given.

L12 ANSWER 14 OF 16 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:359936 HCPLUS

DOCUMENT NUMBER: 133:99079

TITLE: New Anilinophthalazines as Potent and Orally Well Absorbed Inhibitors of the VEGF Receptor Tyrosine Kinases Useful as Antagonists of Tumor-Driven Angiogenesis

AUTHOR(S): Bold, Guido; Altmann, Karl-Heinz; Frei, Joerg; Lang, Marc; Manley, Paul W.; Traxler, Peter; Wietfeld, Bernhard; Brueggen, Josef; Buchdunger, Elisabeth; Cozens, Robert; Ferrari, Stefano; Furet, Pascal; Hofmann, Francesco; Martiny-Baron, Georg; Mestan, Juergen; Roesel, Johannes; Sills, Matthew; Stover, David; Acemoglu,

Figan; Boss, Eugen; Emmenegger, Rene; Laesser,
 Laurent; Masso, Elvira; Roth, Rosemarie; Schlachter,
 Christian; Vetterli, Werner; Wyss, Dominique; Wood,
 Jeanette M.
 CORPORATE SOURCE: Oncology Research and Process Research, NOVARTIS
 Pharma AG, Basel, CH-4002, Switz.
 SOURCE: Journal of Medicinal Chemistry (2000), 43(12),
 2310-2323
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The sprouting of new blood vessels, or angiogenesis, is necessary for any solid tumor to grow large enough to cause life-threatening disease. Vascular endothelial growth factor (VEGF) is one of the key promoters of tumor induced angiogenesis. VEGF receptors, the tyrosine kinases Flt-1 and KDR, are expressed on vascular endothelial cells and initiate angiogenesis upon activation by VEGF. 1-Anilino-(4-pyridylmethyl)-phthalazines, such as CGP 79787D (or PTK787 / ZK222584), reversibly inhibit Flt-1 and KDR with IC₅₀ values < 0.1 μM. CGP 79787D also blocks the VEGF-induced receptor autophosphorylation in CHO cells ectopically expressing the KDR receptor (ED₅₀ = 34 nM). Modification of the 1-anilino moiety afforded derivs. with higher selectivity for the VEGF receptor tyrosine kinases Flt-1 and KDR compared to the related receptor tyrosine kinases PDGF-R and c-Kit. Since these 1-anilino-(4-pyridylmethyl)phthalazines are orally well absorbed, these compds. qualify for further profiling and as candidates for clin. evaluation.
 REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

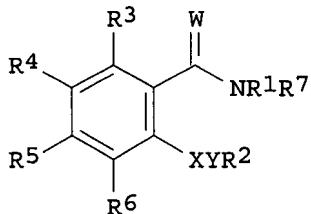
L12 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:335388 HCAPLUS
 DOCUMENT NUMBER: 132:347491
 TITLE: Preparation of N-aryl(thio)anthranilic acid amides as VEGF receptor tyrosine kinase inhibitors
 INVENTOR(S): Altmann, Karl-Heinz; Bold, Guido;
 Furet, Pascal; Manley, Paul William;
 Wood, Jeanette Marjorie; Ferrari, Stefano; Hofmann, Francesco;
 Mestan, Jurgen; Huth, Andreas; Kruger, Martin;
 Seidelmann, Dieter; Menrad, Andreas; Haberey, Martin; Thierauch, Karl-Heinz
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Schering Aktiengesellschaft
 SOURCE: PCT Int. Appl., 77 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027820	A1	20000518	WO 1999-EP8545	19991108
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,			

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2346898	A1	20000518	CA 1999-2346898	19991108
BR 9915210	A	20010724	BR 1999-15210	19991108
TR 200101237	T2	20010821	TR 2001-200101237	19991108
EP 1129075	A1	20010905	EP 1999-971802	19991108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 200104188	A2	20020328	HU 2001-4188	19991108
JP 2002529453	T	20020910	JP 2000-581000	19991108
AU 758230	B2	20030320	AU 2000-13811	19991108
NZ 511339	A	20030725	NZ 1999-511339	19991108
RU 2286338	C2	20061027	RU 2001-114978	19991108
NO 2001001894	A	20010704	NO 2001-1894	20010417
ZA 2001003290	A	20030123	ZA 2001-3290	20010423
MX 2001PA04256	A	20030606	MX 2001-PA4256	20010427
US 2002019414	A1	20020214	US 2001-850434	20010507
US 6448277	B2	20020910		
IN 2001CN00638	A	20050304	IN 2001-CN638	20010508
ZA 2001004673	A	20020909	ZA 2001-4673	20010607
US 2003064992	A1	20030403	US 2002-180289	20020626
US 6878720	B2	20050412		
US 2004198782	A1	20041007	US 2004-828951	20040421
US 7002022	B2	20060221		
US 2006074112	A1	20060406	US 2005-254897	20051020
PRIORITY APPLN. INFO.:				
			GB 1998-24579	A 19981110
			WO 1999-EP8545	W 19991108
			US 2001-850434	A3 20010507
			US 2002-180289	A3 20020626
			US 2004-828951	A3 20040421

OTHER SOURCE(S) : MARPAT 132:347491
GI



AB Use of title compds. I; W = O, S; X = NR8; Y = CR9R10(CH2)n, SO2; R9, R10 = H, alkyl; n = 0-3; R1 = aryl; R2 = mono- or bicyclic heteroaryl with the exception that R2 cannot = 2-phthalimidyl, and when Y = SO2 cannot represent 2,1,3-benzothiadiazol-4-yl; R3-R6 = H, substituent; R7, R8 = H, alkyl; or a N-oxide or a pharmaceutically acceptable salt thereof, for the preparation of a pharmaceutical product for the treatment of a neoplastic disease which responds to an inhibition of the VEGF receptor tyrosine kinase activity is claimed. Thus, a mixture of 4-pyridinecarboxaldehyde and 2-amino-N-(4-trifluoromethylphenyl)benzamide (preparation given) in MeOH containing

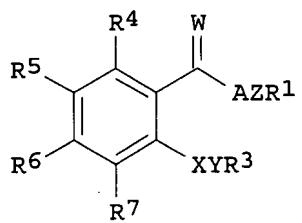
HOAc was treated with NaBH3CN followed by 16 h stirring to give 2-[(4-pyridyl)methyl]amino-N-[4-(trifluoromethyl)phenyl]benzamide. Tested I inhibited Flt-1 VEGF receptor tyrosine kinase with IC50 = 0.18-0.56 μM.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 16 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:335387 HCPLUS
 DOCUMENT NUMBER: 132:334364
 TITLE: Preparation of anthranilic acid amides as vascular endothelial growth factor receptor inhibitors.
 INVENTOR(S): Huth, Andreas; Seidelmann, Dieter; Thierauch, Karl-Heinz; Bold, Guido; Manley, Paul William; Furet, Pascal; Wood, Jeanette Marjorie; Mestan, Jurgen; Bruggen, Jose; Ferrari, Stefano; Kruger, Martin; Ottow, Eckhard; Menrad, Andreas; Schirner, Michael
 PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany; Novartis Aktiengesellschaft
 SOURCE: PCT Int. Appl., 96 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027819	A2	20000518	WO 1999-EP8478	19991109
WO 2000027819	A3	20000817		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
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PRIORITY APPLN. INFO.:			GB 1998-24579	A 19981110
			DE 1999-19910396	A 19990303
			WO 1999-EP8478	W 19991109
			IN 2001-MN422	A3 20010419

OTHER SOURCE(S): MARPAT 132:334364
 GI



AB Title compds. [I; A = NR₂; W = O, S, H₂, NR₈; Z = NR₁₀, N, NR₁₀(CH₂)_q, alkyl, etc.; q = 1-6; AZR₁ = tetrahydroisoquinolinyl, indazolyl, 5-chloroindolyl, etc.; R₁ = (substituted) aryl, heteroaryl; R₂ = H, alkyl; R₃ = (substituted) mono- or bicyclic aryl, heteroaryl; R₄-R₇ = H, halo, (substituted) alkoxy, alkyl, carboxyalkyl; R₅R₆ = dioxetanyl; R₈, R₁₀ = H, alkyl]. Thus, Me N-(4-pyridylmethyl)anthranilate (preparation given) was stirred with Ph(CH₂)₃NH₂ and Me₃Al were stirred in PhMe to give N-(3-phenylprop-1-yl)-N₂-(4-pyridylmethyl)anthranilamide. The latter inhibited VEGFR I with IC₅₀ = 0.05 μM.